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Effectiveness of massage therapy to reduce bilirubin levels in neonates with hyperbilirubinemia a systematic review and metaanalysis

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ABSTRACT

Hyperbilirubinemia in neonates is often a health problem that can cause serious complications such as encephalopathy, kernicterus, and even death if not treated properly. Currently, treatments focus on phototherapy, which despite its positive impact, also has the potential to cause negative effects such as diarrhea, dehydration, skin rash, blue baby syndrome, and skin darkening. Massage therapy is emerging as a potential intervention to reduce the need for phototherapy and lower bilirubin levels. Although massage therapy shows a positive impact, it has not been proven to be fully effective in lowering bilirubin levels in neonates with hyperbilirubinemia. The aim of this systematic review is to assess the effectiveness of massage therapy on reducing bilirubin levels in neonates with hyperbilirubinemia. In this review, 127 articles were selected, and the results showed that massage therapy was effective in reducing bilirubin levels in neonates. In conclusion, massage therapy can be implemented in health services as an effective approach to treat hyperbilirubinemia in neonates.

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1. Introduction

Neonates or also called newborns aged 0-28 days, in newborns hyperbilirubinemia is a common problem (Fonna et al., 2021). Elevated bilirubin levels in newborns can cause very serious health problems such as encephalopathy and kernicterus (Gözen et al., 2019). Hyperbilirubinemia is a total serum bilirubin level ≥ 5 mg/dL (86µmol/L) (Hansen, 2021). Hyperbilirubinemia is a transient condition often found in both full-term (50-70%) and preterm infants (80-90%) (Kemenkes Republik Indonesia, 2019). Most hyperbilirubinemia is physiological and does not require specific therapy, due to the toxic potential of bilirubin, all neonates should be monitored to detect the possibility of severe hyperbilirubinemia (Creeden et al., 2021; Du et al., 2021; Muniyappa & Kelley, 2020; Watson, 2009).

Neonatal hyperbilirubinemia is usually seen in newborns aged 3-7 days and can occur at birth or during the newborn period (Basiri-Moghadam, Basiri-Moghadam, Kianmehr & Jani, 2015). Bilirubin is a breakdown product of hemoglobin, the increase of which in infants can cause deposition on the skin and mucous membranes and lead to jaundice (Suely et al., 2015). High bilirubin levels can lead to dangerous complications such as mental retardation, motor and balance disorders, seizures, hearing loss, speech impairment and others (Wang et al., 2021). Therefore, early diagnosis and treatment of neonatal jaundice

is essential. Several methods are available for the treatment of jaundice, however, the main form of treatment involves the use of phototherapy (Hansen et al., 2020; Namnabati et al., 2018; Shirzadfar & Sheikhi, 2020). Phototherapy is associated with side effects such as temporary skin rashes, mild hyperthermia, and retinal damage (Bienia et al., 2021; Jazayeri et al., 2021; Sead et al., 2020).

On a world scale, the cause of neonatal mortality due to hyperbilirubinemia is quite high at 1309 deaths per 100,000 live births and is the seventh cause of neonatal death (Zhang et al., 2021). Neonatal mortality rate (NMR) is one of the indicators of health status in the Sustainable Development Goal (SDGs) and the National Medium-Term Development Plan (RPJMN) 2015-2019 (Keputusan Mentri Kesehatan Republik Indonesia, 2019). The results of the 2017 Indonesian Demographic and Health Survey (IDHS) showed an IMR of 15 per 1,000 live births, an IMR (Infant Mortality Rate) of 24 per 1,000 live births, and an IMR (Toddler Mortality Rate) of 32 per 1,000 births. The main causes of infant mortality in Indonesia are due to LBW 26%, jaundice 9%, hypoglycemia 0.8% and neonatal infection 1.8% (Kemenkes RI, 2020)

Treatment and management of hyperbilirubin in neonates is currently still focused on treatment ranging from phototherapy to neonatal blood transfusion to prevent the effects of hyperbilirubinemia (Shoris et al., 2023). Each method has positive effects and drawbacks such as diarrhea, unnoticed increase in dehydration, skin rash, blue baby syndrome, and skin darkening while some effects of phototherapy are also debated as phototherapy may cause malignancy in the treatment of neonatal jaundice (Zsanett etal, 2007).

Infant massage is one of the interventions reported to support infant weight gain, positively impact sleep patterns, and reduce the need for phototherapy (Firmino et al., 2022; Mrljak et al., 2022). Infant massage is one method that in addition to helping mothers and infants relax has also been shown to improve parameters such as height, weight, head circumference, bone density, sleep duration, and breathing patterns while reducing the incidence of colic, defecation is a bilirubin removal mechanism, so it is likely to reduce jaundice (Diego et al, 2005).

Infant massage is also useful for controlling bilirubin into normal values, infant care by providing massage on the body can stimulate the vagus nerve and can increase the production of food-absorbing hormones that can increase the secretion of gastric and pancreatic juices and increase the amount of milk sucked by the baby and improve digestive function in babies better (Chen et al., 2011). Although massage therapy has a positive impact, its effectiveness in reducing bilirubin levels in cases of hyperbilirubinemia has not been proven so that its application is still rarely applied in health services, especially in providing nursing care (Sari & Yulianti, 2022; Senbekov et al., 2020; Travers et al., 2020). Therefore, the author is interested in conducting a literature study related to the effectiveness of massage therapy in reducing bilirubin levels in neonates. The aim of this systematic review was to determine the effectiveness of massage therapy on reducing biliribin levels in neonates with hyperbilirubinemia.

2. Methods

The method in this systematic review uses the PRISMA checklist in selecting articles found based on objectives (O'Dea et al., 2021; Sarkis-Onofre et al., 2021). This research article collection is sourced from pubmed, cochrane and proquest, full text using the RCT (Randomized controlled trial) method and based on the PICO format. Articles were analyzed for quality using the JBI format, GRADE approach and assessed for risk of bias.

Eligibility Criteria

This systematic review was selected based on eligibility criteria based on the PICO format as follows:

Table 1.
Eligibility Criteria

Study Design	*Randomized controlled trial*
Article characteristics	Full article International Articles and no time limit on article searches
Population	Inclusion criteria were newborns (neonates) born at 37-41 weeks gestation (full term) who had hyperbilirubin either who were not or were undergoing phototherapy and

	were treated in the hospital, neonates in healthy condition with birth weight ≥2500 and ≤4000 grams. Exclusion criteria were neonates with congenital, biliary atresia, infection and chronic diseases.
Intervention	Massage therapy (massage) performed on the surface of the neonate's skin starting from the legs to the abdomen, hands and back as well as massage performed starting from the face, chest, abdomen, upper and lower extremities and the back using oil.
Comparison	– Standard Operating Procedure (SOP) or standard of care for hospitalized neonates with hyperbilirubin – No intervention
Results	Decreased bilirubin levels.

Population

In this systematic review, the population used was newborns who were treated at the hospital with the inclusion criteria of babies born at 37-41 weeks gestation (full term) who experienced hyperbilirubin either not or undergoing phototherapy, babies with a birth weight of ≥2500 and ≤4000 grams, neonates in good health. Exclusion criteria were infants with congenital abnormalities, biliary atresia, infection, and chronic diseases. Hyperbilirubin in neonates is a condition in neonates characterized by an abnormal increase in bilirubin levels in the blood both conjugated and unconjugated.

3. Results and Discussion

In this systematic review, the intervention used was massage therapy. The massage is done by giving smooth strokes on the surface of the neonate's skin starting from the legs to the abdomen, hands and back as well as massage starting from the face, chest, abdomen, upper and lower extremities and the back using oil.

Comparations

In the systematic review, the comparator of massage therapy intervention is the Standard Operating Procedure (SOP) or standard care for neonate care in hospitals with hyperbilirubin.

Outcome

The outcome of this systematic review is the decrease in bilirubin levels in neonates. Bilirubin levels were measured before and after massage therapy.

Study Design

The study design used in this systematic review is Randomized Controlled Trial (RCT).

Information Source

The databases used in this article search are pubmed, cochrane and proquest.

Data Collection Proces and Data Items

Data obtained by researchers were extracted in name, year, country, title, sample, design, intervention (including massage frequency, comparator), and bilirubin level results. There are seven articles synthesized in this systematic review examined for risk of bias using quality assessment Risk of Bias in randomized trials (ROB 2.0) cochrane domain, then the risk of bias data is input into the revman software to make conclusions in the form of diagrams, namely 7 articles show low risk on random sequence generation indicators (selection bias). 1 article shows unclear risk, 1 hight risk article and 5 low risk articles on the allocation conceal ment indicator (selection risk). 2 articles showed unclear risk, 2 high risk articles and 3 low risk articles on indicators of blinding of participants and personnel (performance bias) and blinding outcome assessment (detection bias). 1 hight risk article and 6 low risk articles on indicators of incomplate outcome data (attrition bias) and selective reporting (reporting bias). 1 article showed high risk and unclear and low risk on other bias indicators.

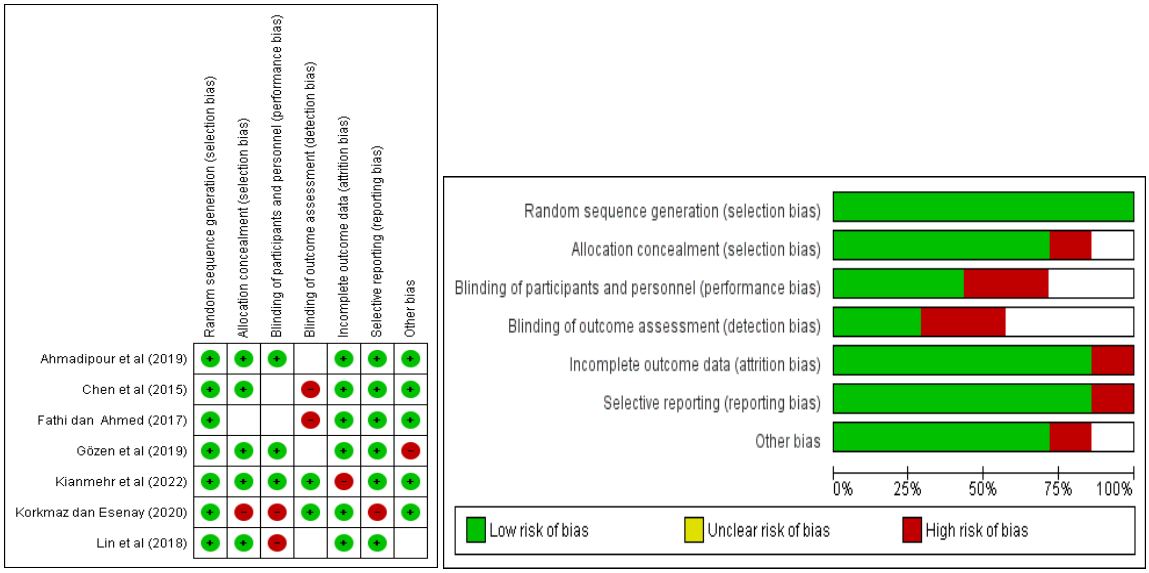

Figure 1. Risk of Bias

Quality of Evidence

The quality assessment of the article was assessed using The Joanna Briggs Instutute (JBI) Critical Appraisal tools Randomized Controlled Trials (RCT) and the Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach. as for the assessment of article quality using JBI, namely:

Table 2.
Quality of Evidence

Joanna Briggs Institute: Randomised Controlled Trial Checklist	Kianmehr et al (2022)	Lin et al (2018)	Korkmaz dan Esenay, (2020)	Fathi dan Ahmed, (2017)	Ahmadipour et al (2019)	Chen et al (2015)	Gözen et al (2019)
Was the randomization used for sample selection done correctly?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the assignment to treatment groups hidden?	Yes	No	No	Unclear	Yes	Yes	Yes
Does the treatment group have similar characteristics to the control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were participants blinded to group assignment?	Yes	Yes	No	Unclear	Yes	Unclear	Yes
Are the blinded outcome assessors unaware of the group assignments?	Yes	Unclear	Yes	Unclear	Unclear	No	Unclear
Were the intervention and control groups given the same treatment other than the intervention?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Are participants randomly analyzed in group assignment?	Yes	Yes	Yes	Yes	Yes	No	Yes
Are outcomes measured in the same way in the treatment group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Are the results measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is the statistical analysis used appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Is the RCT design appropriate for the topic and are there differences in the methods and analyses from standardized RCTs?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	

Table 3.
Article Synthesis Results

No	Researcher and Year	Article Title	Research Design	Sample	Intervention	Comperation	Mean & Std. Deviasi	Results
1.	Kianmehr et al (2022)	*The Effect of Massage on Serum Bilirubin Levels in Term Neonates with Hyperbilirubinemia Undergoing Phototherapy*	*Randomized Control Trial* (RCT) *pre post-post test*	34 neonates who were divided into intervention group (n=18) and control group (n=16) with inclusion criteria of full-term neonates with hyperbilirubin who underwent phototherapy with body weight ranging from 2500 to 4000 grams with bilirubin level of 13-24 mg/dl, neonates who were given breast milk or formula milk and were not undergoing any treatment.	Neonates were given massage intervention along with phototherapy. Massage was done for 15 minutes within 3 consecutive days after 30 minutes of breastfeeding or milk in the morning.	The neonate was treated according to the standard of Bahman Hospital in Gonabad, Iran, i.e., phototherapy alone.	The intervention group before and after the intervention experienced a decrease in bilirubin of 7.83 ± 2.19 while in the control group before and after the intervention experienced a decrease in bilirubin of 6.22 ± 1.75.	After massage for 3 days within 15 minutes, the results showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.001 (<0.05).
2.	Lin et al (2018)	*Effects of Infant Massage on Jaundiced Neonates Undergoing Phototherapy*	*Randomized Control Trial* (RCT)	26 neonates were divided into intervention group (n=15) and control group (n=11) with inclusion criteria of full-term neonates with hyperbilirubin who underwent phototherapy with body weight ranging from 2500 to 3600 grams with bilirubin level > 15 mg/dl, neonates who were given breast milk or formula milk and were not undergoing any treatment.	Neonates were given massage intervention accompanied by phototherapy. The massage was done for 15-20 minutes each massage session. This massage was done 2 times a day after breastfeeding time for 3 consecutive days.	Neonates were treated in accordance with the standards of a regional teaching hospital in Taicung City, Central Taiwan, namely the provision of phototherapy alone.	The intervention group before and after the intervention experienced a decrease in bilirubin by 4.8 ± 0.9 while in the control group before and after the intervention experienced a decrease in bilirubin by 3.7 ± 0.8.	After massage therapy for 3 days within 15-20 minutes twice a day, the results showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.03 (<0.05).
3.	Korkmazdan Esenay, (2020)	*Effects of Massage Therapy on Indirect Hyperbilirubinemia in Newborns Who*	*Randomized Control Trial* (RCT)	50 neonates who were divided into intervention group (n=25) and control group (n=25) with inclusion criteria of full-term neonates with hyperbilirubin	Neonates were given massage intervention with phototherapy. massage was done	Neonates were treated in accordance with the standards of Ankara Hospital, Turkey,	The intervention group before and after the intervention experienced a decrease	After a 15-minute massage twice a day for 2-3 days, the results showed that massage

		Receive Phototherapy		who underwent phototherapy with body weight ranging from 2500 to 4000 grams, neonates who were breastfed or formula fed and were not undergoing any treatment.	for 15 minutes twice a day for 2-3 days depending on phototherapy instruction. Massage was given after 30 minutes of breastfeeding or formula feeding.	namely the provision of phototherapy alone.	in bilirubin by 1.73 ± 0.13 while in the control group before and after the intervention experienced a decrease in bilirubin by 1.02 ± 0.3.	therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.000 (<0.05).
4.	Fathi dan Ahmed, (2017)	*Effect of Infant Massage Oil on Jundiced Neonates Undergoing Phototherapy*	*Randomized Control Trial (RCT)*	80 neonates were divided into intervention group (n=40) and control group (n=40) with inclusion criteria of full-term neonates with hyperbilirubin who underwent phototherapy with body weight ranging from 2500 to 3600 grams, neonates who were breastfed or formula fed and were not undergoing any treatment.	Neonates were given massage intervention accompanied by phototherapy. Massage was done for 15-20 minutes twice a day for 3 consecutive days and phototherapy was stopped during the massage process.	Neonates were given treatment in accordance with hospital standards, namely the provision of phototherapy only.	The intervention group before and after the intervention experienced a decrease in bilirubin by 4.9 ± 0.9 while in the control group before and after the intervention experienced a decrease in bilirubin by 3.7 ± 0.9.	After massage for 15-20 minutes twice a day for 3 days, the results showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.02 (<0.05).
5.	Ahmadipour et al (2019)	*The Lowering of Bilirubin Levels in Full-Term Newborns by the Effect of Combined Massage Therapy and Phototherapy Practice*	*Randomized Control Trial (RCT)*	83 neonates who were divided into intervention group (n=40) and control group (n=43) with inclusion criteria of full-term neonates with hyperbilirubin who underwent phototherapy with body weight ranging from 2500 to 4000 grams who had bilirubin levels of 15-20 mg/dl, neonates who were breastfed or formula fed and were not undergoing any treatment.	Neonates were given massage intervention accompanied by phototherapy. Massage was done for 15 minutes twice a day for 4 consecutive days. Massage was done after 1 hour of neonate breastfeeding.	Neonates were given treatment in accordance with the standards of Shaid Madani Hospital, namely the provision of phototherapy only.	The intervention group before and after the intervention experienced a decrease in bilirubin by 6.0 ± 0.14 while in the control group before and after the intervention experienced a decrease in bilirubin by 5.4 ± 0.8.	After massage for 15 minutes twice a day for 4 days, the results showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.000 (<0.05).
6.	Chen et al (2015)	*Baby Massage Ameliorates Neonatal Jaundice in Full Term*	*Randomized Control Trial (RCT*	44 neonates were divided into intervention group (n=22) and control group (n=22) with inclusion criteria of	Neonates were given massage intervention accompanied by	Neonates were treated in accordance with the standards of Sekizuka	The intervention group before and after the intervention	After massage for 15-20 minutes twice a day for 5 days, the results

		Newborn Infant		full-term neonates with hyperbilirubin who underwent phototherapy with body weight ranging from 2800- 3600 grams, neonates who were breastfed or formula fed and not undergoing any treatment.	phototherapy. Massage was done for 15-20 minutes twice a day for 5 consecutive days. Massage was done after 1 hour of neonate breastfeeding in the morning and afternoon. Neonates were given massage intervention accompanied by phototherapy. The massage was done on the abdomen for 5 minutes for each session, the number of sessions in this massage was 6 sessions that had to be completed within 2 days.	Shibata Hospital in Niigata, Japan, namely the provision of phototherapy alone.	experienced a much lower decrease in total bilirubin with a value of 11.7 ± 2.8 compared to the control group which experienced a decrease in bilirubin of 13.7 ± 1.7.	showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.009 (<0.05).
7.	Gözen et al (2019)	*Transcutaneous Bilirubin Levels of Newborn Infants Performed Abdominal Massage*	*Randomized Control Trial (RCT)*	90 neonates who were divided into intervention group (n=44) and control group (n=46) with inclusion criteria of full-term neonates who had hyperbilirubin with phototherapy with body weight ranging from 2500 to 4000 grams, neonates who were given breast milk/formula milk and were not undergoing any treatment.		Neonates were treated according to the standard of Medipol Hospital, Turkey, i.e. phototherapy only.	The intervention group before and after the intervention experienced a decrease in bilirubin of 1.96 ± 1.69, while the control group before and after the intervention experienced a decrease in bilirubin of 1.80 ± 1.23.	After massage for 5 minutes/session for 6 sessions for 2 days, the results showed that massage therapy was effective in significantly reducing bilirubin levels in neonates with a P value of 0.001 (<0.05).

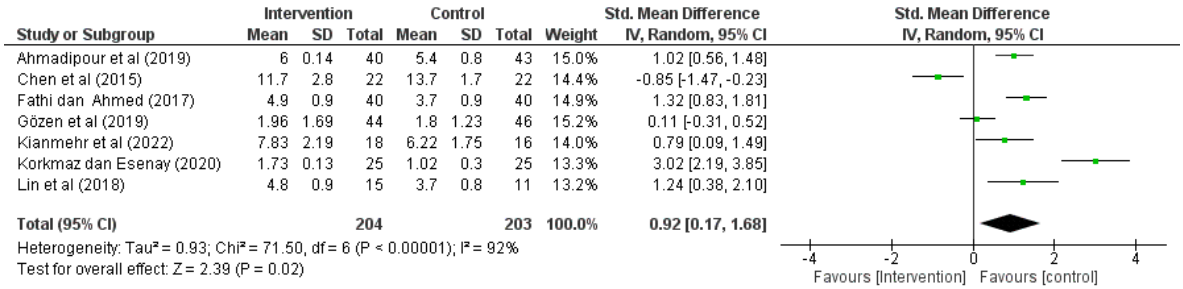

Figure 2. Forest Plot Meta-analysis of Massage Therapy in Lowering Bilirubin Levels in Neonates

Based on the results of metaanalysis on the forest plot, it can be interpreted that the 7 articles have high heterogeneity with a value of (P 0.00001) (P < 0.05) and I2 92% which means that the heterogeneity is also high. Test for overall effect (P 0.02) which means there is a difference between the intervention group and the control group in reducing bilirubin levels in neonates. The 7 articles also show that massage

therapy has a high effect on reducing bilirubin levels in neonates with the results of Std. Mean Difference 0.79-3.02 95% CI (0.09-1.49) to (2.19-3.85).

Discussion

In this review, 7 studies were obtained related to infant massage to reduce bilirubin levels. In the literature study, a sample of infants was taken with the results showing that the duration of massage performed for 15 minutes showed a good reduction in bilirubin levels. But there are those who take the duration of massage 15-20 minutes and there are those who do 5 minutes of each massage session, all of which show the results of bilirubin reduction.

The results of a literature study indicated that infant massage performed 3 times a day showed a significant reduction in bilirubin in infants with a body weight of 2500 - 4000 grams. Infant massage stimulates the newborn and increases readiness to suckle (Gülçin Korkmaz,2019) and the frequency of bowel movements increases as the frequency of breastfeeding increases. Massage accelerates vagal stimulation and decreases bilirubin levels by increasing food intake and bowel movement frequency. besar(Korkmaz & Esenay, 2020). Infant massage is an alternative supporting therapy that is thought to increase bilirubin excretion in infants during Phototherapy, this is because the stimulation can stimulate metabolism so that toxins in the body are easily broken down and excreted through feces and urine, increase the work of digestive organs and swallowing processes in neonates so that there is an increase in metabolism in the body (Benny K, 2022).

From 7 literatures on the results of the intervention, the average decrease in bilirubin levels after infant massage was varied from the start of massage therapy which was carried out for 15 minutes with a duration of 3 times a day there was a decrease in bilirubin 7.83 ± 2.19. (Kianmehr et al., 2022) then in baby massage performed for 15-20 minutes which is done 2 times a day there is a decrease of 4.8 ± 0.9 (Lin et al., 2018) moderate in infant massage performed for 15 minutes with a duration of 2 times a day decreased bilirubin 1.73 ± 0.13 (Korkmaz dan Esenay, 2020). The results of the metanalysis of 7 articles showed that massage therapy had a high effect on reducing bilirubin levels in neonates with a Std. Mean Difference 0.79-3.02 95% CI (0.09-1.49) to (2.19-3.85).

The steps of infant massage carried out from 7 studies also have in common starting with massage starting from the face, preorbital area and cheeks, and then moving towards the chest, then to the abdomen, according to the direction of the colon, namely the nurse massaging gently in a semicircle, next on the limbs, massage with moderate pressure on the outer side of the upper and lower limbs, and finally on the back, and give a massage with two hands from the spine to both sides through the neck to the buttocks. Everything done is very effective in reducing bilirubin levels in infants with hyperbilirubin.

Implications

Based on the synthesized articles, infant massage is very effective in lowering bilirubin levels, reducing the need for phototherapy, increasing infant weight, positively impacting infant sleep patterns and shortening hospital stays. Therefore, the many benefits of infant massage and the application of infant massage are easy to implement in health services and the risks posed by the massage are minimal such as the possibility of allergies on the baby's skin due to massage oil. So this massage therapy can be used as an intervention and implementation in the provision of nursing care for children with hyperbilirubinemia both by nurses and mothers of infants after educating the application of baby massage to nurses.

4. Conclusions

Infant massage has a positive impact on reducing bilirubin levels in cases of hyperbilirubinemia. In addition, infant massage is one of the interventions reported to support infant weight gain, have a positive impact on sleep patterns, and reduce the need for phototherapy so as to reduce the need for hospitalization. The provision of infant massage in infants with hyperbilirubinemia can be optimized by improving one of the interventions and implementation of nursing care and can involve the baby's mother in the intervention process. In future research, I aim to explore the long-term effects of incorporating infant massage as a complementary intervention in the care of neonates with hyperbilirubinemia. This

study will focus on assessing the impact of regular massage on bilirubin levels, weight gain, sleep patterns, and the need for phototherapy, with a particular emphasis on reducing the necessity for hospitalization. By optimizing the implementation of nursing care and actively involving the infants' mothers in the massage intervention, this research seeks to establish evidence-based practices that enhance the overall well-being of neonates with hyperbilirubinemia. The goal is to contribute valuable insights to the development of holistic and patient-centered approaches in neonatal care, promoting a more comprehensive understanding of the potential benefits of infant massage in conjunction with standard medical interventions.

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