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A Study on the Physiological Obstructive Jaundice in Diwaniya

A project

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وزارة التعليم العالي والبحث العملي جامعة القادسية كلية الصيدلة فرع العلوم والمختبرات السريرية

دراسة عن اليرقان الانسدادي الفسيولوجي في الديوانية

بحث مقدم الى كلية الصيدلة وجامعة القادسية كجزء من متطلبات نيل درجة البكالوريوس الصيدلة

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1.11

بسْم اللَّوالرَّحْمَنِ الرَّحِيم وَعَلَّمُ ادْمُرَالْأُسْمَاءَ كَلْهَا ثُعَرَّعَهُ صُهُدُعَكَه المكائكة فقال أنبنوني بأسماء هؤلاء إن كنتم صادقينَ (٣١) قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا 5 إِنَّكَ أَنتَ الْعَلِيمُ الْحَصِيم

صدقاللهالعلىالعظيم

Dedication

To my family...

To our neonatal jaundice patient in Iraq...

To everyone help me...

List of contents

ПО	subject	page
	List of contents	
	Abstract	
	Chapter one	
1.1	jaundice	1
	Chapter two	
2.1	Neonatal jaundice	4
2.2	Signs and symptoms	4
2.3	Causes	4
2.3.1	Unconjugated	7
2.3.2	Conjugated (Direct)	
2.4	Diagnosis	12
2.5	Treatment	13
2.6	Complications	14
	Chapter three	
3.1	Results and discussion	15
	Chapter four	
4.1	References	18

Summery

The study was conducted at the pediatric and obstetrics Hospital in Diwaniyah for children with jaundice (physiological). The study included 100 samples of children infected between the beginning of December 2017 and the end of February 2018. The results were high percentage of bilirubin in infected children, TSB17 mg / dl the results showed that the incidence of male infection was higher than that of females. The results showed that most cases were on the second day of birth. Signs of the disease appeared on the third day of birth, such as yellowing of the nose and eye. They relied on breast milk and did not feed on breast milk, which led to a rise in the proportion of bilirubin in the blood of children infected more than children who breastfeed and infected with the disease.(Glucose and amphetamine and caramycin) to avoid further complications of the disease and most of the weights of children infected and close to the ages of mothers are limited (20-30) and was the blood group of the affected children.

Aim of the study

1 - The study aims to know the number of children with jaundice in the city of Diwaniyah where the results showed a high percentage of children with jaundice disease (physiological) during the study period

2 - Knowledge of the relationship between the nutrition of the newborn child and jaundice (Physiological) where the study showed the high proportion of bilirubin children with jaundice who rely on artificial milk compared to children infected who rely on breast milk

3 - Knowledge of differences in the rate of infection between males and females The study showed that the number of males with jaundice more than females during the study period

4-Knowing the most important treatments and successful in the treatment of the disease

الخلاصة

اجريت هذة الدراسة في مستشفى الولادة والاطفال في الديوانية للأطفال المصابين باليرقان الولادي (الفسيولوجي) وقد جمعت 100 عينه من الاطفال المصابين ما بين فترة بداية شهر كانون الاول سنة ٢٠١٧ الى نهاية شهر شباط ٢٠١٨ وقد كانت النتائج ارتفاع نسبة البيلروبين عند الاطفال المصابين وقد كانت اعلى نسبه للmg/dl ٢٧ TSB واظهرت النتائج ان نسبة الاصابة بالذكور كانت اعلى من الاناث واظهرت النتائج ان معظم حالات الاصابة كانت في اليوم الثاني من الولادة وظهرت علامات المرض في اليوم الثالث من الولادة مثل اصفرار الاصابة كانت في اليوم الثاني من الولادة وظهرت علامات المرض في اليوم الثالث من الولادة مثل اصفرار الاصابة كانت في اليوم الثاني من الولادة وظهرت علامات المرض في اليوم الثالث من الولادة مثل اصفرار الاصابة كانت في در النتائج ايضا ان معظم الاطفال المصابين في المرض كانوا يعتمدون على الرضاعة الحليب الاصطناعي ولم يتغذون على الحليب الام مما ادى الى ارتفاع نسبة البيلروبين في دم الاطفال المصابين اكثر من الاطفال الذي يرضعون حليب الام والمصابين بالمرض ايضا وكانت اكثر الطرق المتبعة في المستشفى والكر من الاطفال الذي يرضعون حليب الام والمصابين بالمرض ايضا وكانت اكثر الطرق المتبعة في المستشفى العلاج الاطفال الذي يرضعون حليب الام والمصابين بالمرض ايضا وكانت الموان الموابين المنوبين في دم الاطفال المصابين العر من الاطفال الذي يرضعون حليب الام والمصابين بالمرض ايضا وكانت اكثر الطرق المتبعة في المستشفى المولي من الاطفال الذي يرضعون حليب الام والمصابين بالمرض ايضا وكانت الحيوية الاخرى (الكلوكوز وامبسلين والكرامايسين) لتفادي حصول مضاعفات اخرى للمرض وكانت معظم اوزان الاطفال المصابين متقاربة واعمار

الهدف من الدر اسة

١-تهدف الدراسة الى معرفة اعداد الاطفال المصابين بمرض اليرقان الولادي في مدينة الديوانية حيث اظهرت النتائج الى ارتفاع نسبة الاطفال المصابين بمرض اليرقان الولادي (الفسيولوجي) خلال فترة الدراسة

٢- معرفة العلاقة بين تغذية الطفل حديث الولادة واليرقان الولادي (الفسيولوجي) حيث اظهرت الدراسة ارتفاع نسبة صبغة البيلروبين عند الاطفال المصابين باليرقان الذين يعتمدون على الحليب الاصطناعي مقارنة بالأطفال المصابين الام

٣- معرفة الفروقات في معدل الاصابة بين الذكور والاناث واظهرت الدراسة ان عدد الذكور المصابين باليرقان اكثر من الاناث خلال فترة الدراسة

٤ ـ معرفة اهم العلاجات وانجحها في علاج المرض



1.1 Jaundice

Jaundice is not a disease in itself, but it is a health problem caused by the high level of bilirubin in the blood, which earns the skin and eyes and mucous membranes yellow color, and the high level of bilirubin in the blood may be caused by the decomposition of blood corpuscles significantly cannot get rid of the liver speed required to accumulate in or due to the presence of a disease or problem in the liver, which makes it unable to rid the body of this substance and accumulate in the blood as well. [1] the most common cases of neonatal jaundice[2], and when untreated, become a disease affecting the central nervous system. Jaundice is observed in the first week in 60% of newborns and 80% in preterm infants [3] 50% of newborns are infected with jaundice during the first week of birth. therefore, it is called physiological jaundice, which is normal due to the increase in the proportion of bilirubin in the blood, which is the pigment of yellow in the blood of all newborns and resulting from the collapse of fetal hemoglobin in red blood cells and hemoglobin which occur physiologically in all newborns the incidence of neonatal newborns in jaundice is not a matter of concern, and in most cases does not require treatment, and the most important reasons: [4] the rate of decomposition of red blood cells in newborns is higher than in adults, so the production of bilirubin have higher than leading to their accumulation. the liver is the main organ responsible for the elimination of bilirubin, but may be incomplete in newborns and is still growing and unable to get rid of the accumulated amount of bilirubin in the blood. usually the liver works to rid the body of bilirubin through its secretion in the form of gall bladder juice in the intestine and then exit with the stool, but in newborns the intestine may re-absorb bilirubin instead of leaving the stool with the outside of the body. for children, there are different types of jaundice that may occur: [5] physiological or natural jaundice: most newborns develop jaundice, which appears as mild yellowing in the body two to four days after birth. any concern is caused by incomplete liver as It is still growing, and this type

Chapter one

introduction

of jaundice disappears on its own within one to two weeks of birth. Jaundice associated with early delivery: It is common in cases of premature birth in which the fetus did not complete the month of pregnancy, and the main reason is the inability of the body of the child is not mature to get rid of bilirubin, and to avoid any complications are treated these children even if the level of bilirubin is less than it in children who have completed the months of pregnancy and have symptoms of natural jaundice. Jaundice associated with breastfeeding: lack of access to the newborn child enough milk may lead to the emergence of symptoms of jaundice, which is not the result of a problem in breast milk, but not to get enough of the child, for the difficulty in the process of breastfeeding or lack of milk secretion of the breast the mother in the quantity required, in this case can resort to breast-feeding or consult with the doctor in the matter. Jaundice associated with breast milk: this type of jaundice occurs in 1-2% of children who rely on breastfeeding, which is the result of the presence of substances in breast milk inhibits the work of the intestines in the elimination of bilirubin, and thus increase in the body and the incidence of jaundice, and notes sperm appears 3 to 5 weeks after initiation of breastfeeding and gradually decreases spontaneously within 3-12 weeks, and there is no need to stop breastfeeding in such a case. treatment of jaundice in children as mentioned above, most cases of jaundice in children from newborns are simple cases and disappear on their own without the need for treatment, but can be followed by some procedures to alleviate the situation, which are: [3] [4] continue breastfeeding from the mother and daily breastfeeding. breastfeeding stimulates bowel movements, thus eliminating bilirubin, which causes jaundice through the stool. the use of light therapy to expose the child to a certain light (not the neon light), taking into account the coverage of the eye and genitalia so that it is shed directly on the skin, breaking the bilirubin, and advised to expose the child to the sun in the early morning; about ten minutes. switching the blood through the withdrawal of a small amount of blood of the child through a device dedicated to it, and then be purified blood from excess bilirubin and then be returned

Chapter one

introduction

back to the body of the child, may need to change the blood more than once according to the rate of elevation in the level of bilirubin we avoid brain damage, and this type of treatment is used in case of phototherapy failure[6].



2.1 Neonatal jaundice

Neonatal jaundice may include seizures, cerebral palsy, or kernicterus.^[7] in many cases there is no specific underlying disorder (physiologic).^[8] In other cases it results from red blood cell breakdown, liver disease, infection, hypothyroidism, or metabolic disorders (pathologic).^{[8][7]} a bilirubin level more than 34 µmol/l (2 mg/dL) may be visible.^[1] Concerns, in otherwise healthy babies, occur when levels are greater than 308 µmol/L (18 mg/dL), jaundice is noticed in the first day of life, there is a rapid rise in levels, jaundice lasts more than two weeks, or the baby appears unwell.^[7] in those with concerning findings further investigations to determine the underlying cause are recommended.^[7] the need for treatment depends on bilirubin levels, the age of the child, and the underlying cause.^{[7][9]} treatments may include more frequent feeding, phototherapy, or exchange transfusions.^[7] in those who are born early more aggressive treatment tends to be required.^[7] Physiologic jaundice generally lasts less than seven days.^[7] The condition affecting over half of babies in the first week of life.^[7] of babies that are born early about 80% are affected.^[8]

2.2 Signs and symptoms

The primary symptom is yellowish discoloration of the white part of the eyes and skin in a newborn baby.^[7] Other symptoms may include excess sleepiness or poor feeding. a bilirubin level more than 34 μ mol/l (2 mg/dL) may be visible. For the feet to be affected level generally must be over 255 μ mol/l (15 mg/dL).^[7]

2.3 Causes

In newborns, jaundice tends to develop because of two factors—the breakdown of fetal hemoglobin as it is replaced with adult hemoglobin and the relatively immature metabolic pathways of the liver, which are unable to conjugate and so excrete bilirubin As quickly as an adult. This causes an accumulation of bilirubin in the blood (hyperbilirubinemia), leading to the symptoms of jaundice [9].

If the neonatal jaundice does not clear up with simple phototherapy, other causes such as biliary atresia, Progressive familial intrahepatic cholestasis, bile duct paucity, alagille syndrome, alpha 1-antitrypsin deficiency, and other pediatric liver diseases should be considered. the evaluation for these will include blood work and a variety of diagnostic tests. prolonged neonatal jaundice is serious and should be followed up promptly. severe neonatal jaundice may indicate the presence of other conditions contributing to the elevated bilirubin levels, of which there are a large

variety of possibilities (see below). these should be detected or excluded as part of the differential diagnosis to prevent the development of complications. they can be grouped into the following categories[9]:



Chapter two

review

2.3.1 Unconjugated

Hemolytic

Intrinsic causes of hemolysis

Membrane conditions

- \circ spherocytosis
- hereditary elliptocytosis
- enzyme conditions
 - glucose-6-phosphate dehydrogenase deficiency (also called G6PD deficiency)
 - Pyruvate kinase deficiency
- globin synthesis defect
 - sickle cell disease
 - alpha-thalassemia, e.g. HbH disease[8]

Extrinsic causes of hemolysis

systemic conditions

- sepsis
- arteriovenous malformation
- alloimmunity (The neonatal or cord blood gives a positive direct coombs test and the maternal blood gives a positive indirect Coombs test)
 - \circ hemolytic disease of the newborn (ABO)^[10]
 - \circ Rh disease^[10]

Chapter

two

review

- hemolytic disease of the newborn (anti-Kell)
- hemolytic disease of the newborn (anti-Rhc)
- o other blood type mismatches causing hemolytic disease of the newborn[10]

Non-hemolytic causes

breastfeeding jaundice

- breast milk jaundice
- cephalohematoma
- polycythemia
- urinary tract infection
- sepsis
- hypothyroidism
- gilbert's syndrome
- crigler-Najjar syndrome
- high GI obstruction (Pyloric stenosis, Bowel obstruction)[10]

2.3.2 Conjugated (Direct)

liver causes Infections

- sepsis
- hepatitis A
- hepatitis B
- tORCH infections

Chapter two

• Metabolic

- galactosemia
- alpha-1-antitrypsin deficiency, which is commonly missed, and must be considered in DDx
- cystic fibrosis
- dubin-Johnson Syndrome
- rotor syndrome
- drugs
- total parenteral nutrition
- idiopathic

Post-liver Biliary atresia or bile duct obstruction

- alagille syndrome
- choledochal cyst

Non-organic causes

Breastfeeding jaundice

"Breastfeeding jaundice" or "lack of breastfeeding jaundice," is caused by insufficient breast milk intake,^[11] resulting in inadequate quantities of bowel movements to remove bilirubin from the body. This leads to increased enterohepatic circulation, resulting in increased reabsorption of bilirubin from the intestines.^[12] usually occurring in the first week of life, most cases can be ameliorated by frequent breastfeeding sessions of sufficient duration to stimulate adequate milk production.

Chapter two

Breast milk jaundice

whereas breastfeeding jaundice is a mechanical problem, breast milk jaundice is a biochemical occurrence and the higher bilirubin possibly acts as an antioxidant. breast milk jaundice occurs later in the newborn period, with the bilirubin level usually peaking in the sixth to 14th days of life. this late-onset jaundice may develop in up to one third of healthy breastfed infants.^[12]

- First, at birth, the gut is sterile, and normal gut flora takes time to establish. the bacteria in the adult gut convert conjugated bilirubin to stercobilinogen which is then oxidized to stercobilin and excreted in the stool. in the absence of sufficient bacteria, the bilirubin is de-conjugated by brush border β-glucuronidase and reabsorbed. this process of re-absorption is called enterohepatic circulation. it has been suggested that bilirubin uptake in the gut (enterohepatic circulation) is increased in breast fed babies, possibly as the result of increased levels of epidermal growth factor (EGF) in breast milk.^[13]breast milk also contains glucoronidase which will increase deconjugation and enterohepatic recirculation of bilirubin.
- Second, the breast-milk of some women contains a metabolite of progesterone called 3-alpha-20-beta pregnanediol. this substance inhibits the action of the enzyme uridine diphosphoglucuronic acid (UDPGA) glucuronyl transferase responsible for conjugation and subsequent excretion of bilirubin. in the newborn liver, activity of glucuronyl transferase is only at 0.1-1% of adult levels, so conjugation of bilirubin is already reduced. further inhibition of bilirubin conjugation leads to increased levels of bilirubin in the blood.^[14] however, these results have not been supported by subsequent studies.[15]

• Third, an enzyme in breast milk called lipoprotein lipase produces increased concentration of nonesterified free fatty acids that inhibit hepatic glucuronyl transferase, which again leads to decreased conjugation and subsequent excretion of bilirubin.^[16]

Physiological jaundice

most infants develop visible jaundice due to elevation of unconjugated bilirubin concentration during their first week. this is called physiological jaundice. this pattern of hyperbilirubinemia has been classified into two functionally distinct periods.

- Phase one
- 1. term infants jaundice lasts for about 10 days with a rapid rise of serum bilirubin up to 204 μ mol/l (12 mg/dL).
- 2. Preterm infants jaundice lasts for about two weeks, with a rapid rise of serum bilirubin up to 255 μ mol/l (15 mg/dL).
- Phase two bilirubin levels decline to about 34 µmol/l (2 mg/dL) for two weeks, eventually mimicking adult values.
- 1. Preterm infants phase two can last more than one month.
- 2. Exclusively breastfed infants phase two can last more than one month.

Mechanism involved in physiological jaundice are mainly:

relatively low activity of the enzyme glucuronosyltransferase which normally converts unconjugated bilirubin to conjugated bilirubin that can be excreted into the gastrointestinal tract.^[17] Before birth, this enzyme is actively down- regulated, since bilirubin needs to remain unconjugated in order to cross the placenta to avoid being accumulated in the fetus.^[18] after birth, it takes some time for this enzyme to gain function.

Chapter two

review

shorter life span of fetal red blood cells,^[16] being approximately 80 to 90 days in a full term infant,^[14] compared to 100 to 120 days in adults.

• relatively low conversion of bilirubin to urobilinogen by the intestinal flora, resulting in relatively high absorption of bilirubin back into the circulation.^[16]

2.4 Diagnosis

diagnosis is often by measuring the serum bilirubin level in the blood.^[9] in those who are born after 35 weeks and are more than a day old transcutaneous bilirubinometer may also be used. the use of an icterometer, a piece of transparent plastic painted in five transverse strips of graded yellow lines, is not recommended.^[9]

Transcutaneous bilirubinometer

this is hand held, portable and rechargeable but expensive. when pressure is applied to the photoprobe, a xenon tube generates a strobe light, and this light passes through the subcutaneous tissue. the reflected light returns through the second fiber optic bundle to the spectrophotometric module. the intensity of the yellow color in this light, after correcting for the hemoglobin, is measured and instantly displayed in arbitrary units.

Pathological jaundice

any of the following features suggests pathological jaundice:

- 1. clinical jaundice appearing in the first 24 hours or greater than 14 days of life.
- Increases in the level of total bilirubin by more than 8.5 μmol/l (0.5 mg/dL) per hour or (85 μmol/l) 5 mg/dL per 24 hours.
- 3. total bilirubin more than 331.5 μ mol/l (19.5 mg/dL) (hyperbilirubinemia). direct bilirubin more than 34 μ mol/l (2.0 mg/dL) the signs which help detect pathological jaundice are the presence of intrauterine growth restriction, stigma

Chapter two

review

of intrauterine infections (e.g. cataracts, small head, and enlargement of the liver and spleen), cephalohematoma, bruising, signs of bleeding in the brain's

4. ventricles. history of illness is noteworthy. family history of jaundice and anemia, family history of neonatal or early infant death due to liver disease, maternal illness suggestive of viral infection (fever, rash or lymphadenopathy), maternal drugs (e.g. sulphonamides, anti-malarials causing red blood cell destruction in G6PD deficiency) are suggestive of pathological jaundice in neonates.^[19]

2.5 Treatment

the bilirubin levels for initiative of phototherapy varies depends on the age and health status of the newborn. however, any newborn with a total serum bilirubin greater than $359 \ \mu mol/l$ ($21 \ mg/dL$) should receive phototherapy.^[20]

Phototherapy

babies with neonatal jaundice may be treated with colored light called phototherapy, which works by changing trans-bilirubin into the water-soluble cis-bilirubin isomer.^{[21][22][23]} the phototherapy involved is not ultraviolet light therapy but rather a specific frequency of blue light. the light can be applied with overhead lamps, which means that the baby's eyes need to be covered, or with a device called a biliblanket, which sits under the baby's clothing close to its skin.^[21]

first discovered, accidentally, at Rochford Hospital in essex, england, when nurses there noticed that babies exposed to sunlight had less jaundice, and pathologists noticed that a vial of blood left in the sun had less bilirubin. a landmark randomized clinical trial published in the *Pediatrics* in 1968; it took another ten years for the practice to become established.^{[22][21]}

Chapter two

review

Exchange transfusions

much like with phototherapy the level at which exchange transfusion should occur depends on the health status and age of the newborn. it should however be used for any newborn with a total serum bilirubin of greater than 428 μ mol/l (25 mg/dL).^{[20][22]}

Alternative therapy

homeopathy, acupuncture, and traditional chinese medicine should not be used.^[3]

2.6 Complications

prolonged hyperbilirubinemia (severe jaundice) can result in chronic bilirubin encephalopathy (kernicterus).^{[24][25]} quick and accurate treatment of neonatal jaundice helps to reduce the risk of neonates developing kernicterus.^[26]

infants with kernicterus may have a fever^[27] or seizures.^[28] high pitched crying is an effect of kernicterus. scientists used a computer to record and measure cranial nerves 8, 9 and 12 in 50 infants who were divided into two groups equally depending upon bilirubin concentrations. of the 50 infants, 43 had tracings of high pitched crying.^[29] exchange transfusions performed to lower high bilirubin levels are an aggressive treatment.^[30]



Result and Discussion

Table (1) shows the age of children at the onset of jaundice. the most common day of the onset of jaundice was the second day of the child's life. The number of infections increased in the second and third days and reached a peak in the second and fourth days. Of the child's age, 95% with an average mean of 6.7, and a standard deviation of 4.9. the table showed that the percentage of males was more than females

The child 's	Number	Number	Percentage
age in days	male	female	
	infection	infection	
Frist day	٧	٤	First week
Second day	۲.	١.	95%
Third day	١٣	٧	
Forth day	11	٦	
Five day	٨	٤	
Six day	۲	٢	
Seven day	١	-	
Eight day	۲	١	%00
Nine day	١	١	
Percentage	%٦٥	%70	
Average	٧,٢	٣٫٨	
mean			
standard	٦,١	۲٫۸	
deviation			

Table (1) shows the age of the child at the onset of jaundice:

Newborn babies are infected with jaundice during the first week of birth, so it is called physiological jaundice, which is normal due to the increase in the proportion of bilirubin in the blood, which is the pigment of yellow in the blood of all newborns resulting from the breakdown of embryonic hemoglobin in red blood cells and Physiology occurs in all newborns the reason for the increase in bilirubin is to break the red blood cells from the normal limit, which leads to the increase of the color of bilirubin and because of the inability of the liver cells to remove them and rid the body of them so the spread of pigment in the blood that break the red blood cells leads to the decomposition of hemoglobin to the part of the kidneys and hemoglobin may increase the symptoms of anemia, and liver enzymes may be incomplete or unstable, especially in preterm infants with high jaundice. in other words, the enzyme is ineffective the three-dimensional form is incomplete. Death as a result of a defect in the process of modification post-translation [31,32] and since bilirubin is soluble in fat so it is not scarified by urine or transmitted by blood except by union with special proteins found in the blood and the liver is converted into a soluble compound This is the case for days or weeks until the end of the excess fetal erythrocytes in the body without the need for treatment. The rate of production of bilirubin in newborns is (8-10) mg Per kg of child weight in 24 hours which is (2-2.5) of the time of the rate of production in adults [33] in normal cases, the level of interaction of bilirubin serum cord is (1-3 mg/dl) and climb to the rate of less than 5 Mg / dl in 24 hours and thus becomes jaundice visible on the second and third days and peaks between the second day and The fourth is an average of 5-6 mg / dl then falls below the rate of 2 mg / dl between the fifth and seventh day. we note from Table (2) which shows the type of nutrition that children relied on The level of bilirubin in children is less natural breastfeeding than children dependent on breast feeding,

Table

(۲)

Age child	Bilirubin percentage					
	Breastfeeding	/ Industrial				
	breastfeeding					
First day	(10-11) mg/dl	(10-11) mg/dl				
Second day	(10-12) mg/dl	(10-13) mg/dl				
Third day	(12-13) mg/dl	(12-13) mg/dl				
Fourth day	(10-9) mg/dl	(14-16) mg/dl				
Five day	(10-8) mg/dl	(14-17) mg/dl				
Six day	(9-8) mg/dl	(14-15) mg/dl				
Seven day	7 mg/dl	(12-14) mg/dl				

shows the relationship between child nutrition and bilirubin

especially in the first five days of life and is believed to be due to the low amount of fluids and calories taken by the child in artificial feeding not to take the substance of colic and also increases the hepatic cycle due to lack of feces and the lack of betaglucuronidase in breast milk [34] It is important when the onset of jaundice that the mother breastfeed her baby at least continuously every two hours, helping to get rid of excessive bilirubin by increasing the movement of the bowel and prevents the reabsorption of bile [35] The researchers found that the child who breastfeed eight times a day has a level of bilirubin three times lower than children who feed less times also affects bilirubin and break the skin when exposed to light to expose the child to indirect sunlight and thus lower level bilirubin[36].



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