

## Recommendations:

Good maternal (prenatal) and neonatal care. Genetic counseling should be an essential part in consanguineous marriage.

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hemolytic disease was reported to be 276 per 100,000 live births worldwide in 2010, translating to 373,300 babies. South Asia, sub-Saharan Africa and Eastern Europe/Central Asia had the highest estimated prevalence rate, roughly 386 per 100,000 live births. In contrast, the estimated prevalence in high-income countries with well-established health-care infrastructure for pregnant females was 2.5 per 100,000 live births.

The prevalence of Rh incompatibility as cause of neonatal jaundice was 5.4% in Bangladeshi infants, similar to that in Turkey. This rate in Makkah, Saudi Arabia, was 2.6%. G6PD deficiency was another identified neonatal jaundice in our study estimated to have a prevalence rate of 4.14% among Egyptian neonates, close to the prevalence rate in Iranian newborn was 6.3%. but among Turkish newborns was 0.5%. On the other hand, G6PD deficiency had a rate of 10.5% among patient neonates in Makkah, Saudi Arabia. In India, this rate was reported as 2.5% in the patients with indirect hyperbilirubinemia.

Severe hyperbilirubinemia due to G6PD deficiency was seen among 21.5% of the neonates in a study from Canada. G6PD deficiency can cause kernicterus with permanent neurologic sequelae in the neonates with severe jaundice, so its early management is important.

A study from Lebanon stated that urinary tract infection was found in 20.1% of the jaundiced newborns, which was about four-fold higher than that in Iran. A higher rate of 18% was reported among Turkish neonates as well. This rate was 6.5% in a survey from Greece, which was near our results. Sepsis was diagnosed in 45% of the patient newborns in a research from Nigeria, which was much higher than our estimated rate of 15.2%.

Jaundice treated by conventional phototherapy in the present meta-analysis 3 studies were analyzed with total number of cases 963. The proportion was 87.34%.

Jaundice treated by exchange transfusion in the present meta-analysis 3 studies were analyzed with total number of cases 963. The proportion was 16.62%.

Total serum bilirubin before and after conventional phototherapy; in the present meta-analysis 2 studies were analyzed with total number of cases 320. Total random effect (SMD=8.003, SE=0.335).

Total serum bilirubin before and after intensive/LED phototherapy; in the present meta-analysis 2 studies were analyzed with total number of cases 320. Total random effect (SMD=10.03, SE=2.64).

In a single blinded randomized control trial from **Coastal India** (2019) comparing Light Emitting Diode (LED) phototherapy versus conventional phototherapy in treatment of neonatal hyperbilirubinemia; 166 neonates  $\geq$  35 weeks of age requiring phototherapy were recruited and further divided into 2 groups [LED (83) and conventional (83)] by using computer generated random numbers. Serial total serum bilirubin levels and random urinary lumirubin levels were collected and side effects of phototherapy were noted. Rate of fall in total serum bilirubin levels (TSB,  $\mu\text{mol/L/hour}$ ) and random urinary lumirubin levels were computed. Significant difference was documented in mean rate of decrease of TSB ( $\mu\text{mol/L/hour}$ ) in LED group ( $5.3 \pm 2.91$ ) when compared to conventional group ( $3.76 \pm 2.39$ ) ( $p < 0.001$ ). (Gutta et al., 2019) this goes with the results of our study.

## Conclusion:

In the present meta-analysis study, phototherapy is the most continent and safe therapeutic method which is used in the first step of treatment of unconjugated neonatal jaundice. It lowers the levels of serum bilirubin and decreases the need for the potentially more invasive therapeutic approach, exchange transfusion.

## Discussion:

The aim of the present study is to establish evidence based neonatal jaundice in Egyptian neonates to assess systematically available evidence on causes, risk factors and management of jaundice in Egypt. Also, the study will provide meaningful information to policy makers and health care professionals to guide decision-making processes.

Using meta-analysis, this study is based on previous Egyptian studies, theses, papers. Data were collected, 32 studies were selected, involved 3458 neonates.

The Mean gestational age in weeks, post natal ages in days, birth weight in kilogram, maternal age in years, APGAR score, serum bilirubin for case and control on admission and discharge were demonstrated.

Birth weight in the present meta-analysis 28 studies were analyzed with total number of 2564. The mean was  $2.961 \pm .3059$  Kgm.

**Formula fed** in the present meta-analysis, 7 studies were analyzed with total number of cases 465. The proportion is 35.67%.

**Maternal parity** in the present meta-analysis, 2 studies were analyzed with total number of cases 111. The proportion is 6.41%.

**Moawad et al. (2015)** provided insight into maternal sociodemographic factors as determinants of knowledge and attitudes related to NNJ in Egypt. Maternal age, education, working status, parity, and residence had a strong influence on the knowledge level and behavior. Although not statistically significant, they found more accurate knowledge and a relatively safe behavior among mothers with parity of  $\geq 3$  and maternal age of  $\geq 35$  years, a finding replicated in other comparable studies. They also found that working mothers and those residing in urban areas were significantly ( $P < 0.05$ ) more likely to have perception and attitudes better than housewives and rural mothers.

Similar findings were reported in studies conducted in India, Sri Lanka and Nigeria. A recent Egyptian survey has found that only 49% of women in rural Upper Egypt receiving regular maternal care, compared with 75% in Upper Egypt urban areas.

Among 32 articles were finally included, the overall pooled prevalence of causes of jaundice among Egyptian neonates were: ABO incompatibility (36.3%), rh-incompatibility (16.29%), cephalhematoma (6.52%), G6PD deficiency (4.14%), other causes (55.3%).

Unknown factors were the most frequent causes of jaundice in Iranian newborns (50.7%). Among known etiologies, ABO blood groups incompatibility has the highest rate of prevalence (16.9%). In a recent national report from Turkey, ABO incompatibility was responsible for jaundice in 21.3% of the neonates, which was close to our results. In a study from Bangladesh, ABO incompatibility was found as the most common cause of hemolytic jaundice (11.3%). On the other hand, this rate was 31.6% in Makkah, Saudi Arabia, which was so close our results.

ABO incompatibility was attributed to jaundice among 15% of newborns in a study and 35% in another study from India. ABO incompatibility is observed when the mother has blood group O and the infant has blood type A or B. Maternofetal ABO incompatibility happens in about 15% of pregnancies, but hemolytic disease of the newborn develops in only 5%.

In the United States, mother-infant ABO incompatibility is seen in 6.9% of all deliveries, and ABO hemolytic disease of the newborn is the most frequent cause of neonatal icterus.

Icterus caused by ABO hemolytic disease is detected within the first 12–24 hours of life; therefore, it is recommended to implement a screening program for all pregnant females. Rh blood group incompatibility as a cause of icterus was estimated among 4% of newborn patients in Iran. In a recent global systematic analysis, the estimated prevalence of Rh

Table (6) shows cases with jaundice treated by conventional phototherapy in 3 studies were analyzed with total number of cases 963. The proportion was 87.34%.

**Table 6: Meta-analysis proportion of jaundiced cases treated by conventional phototherapy**

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Kelany SH, Abd EL Meguid EM, Iskander FI,etal. 2015	55	38.182	25.409 to 52.274	5.80	32.75
Hassan MN, EL Hawary MI,EL Raziky EM,etal. 2009	808	97.772	96.502 to 98.674	83.75	33.95
Badr Eldeen ME,EL Shazly BL, Gad IE.2014	100	100.000	96.378 to 100.000	10.46	33.31
Total (fixed effects)	963	96.629	95.288 to 97.675	100.00	100.00
Total (random effects)	963	87.347	53.709 to 99.956	100.00	100.00

**Test for heterogeneity**

Q	126.2850
DF	2
Significance level	P < 0.0001
I <sup>2</sup> (inconsistency)	98.42%
95% CI for I <sup>2</sup>	97.19 to 99.11

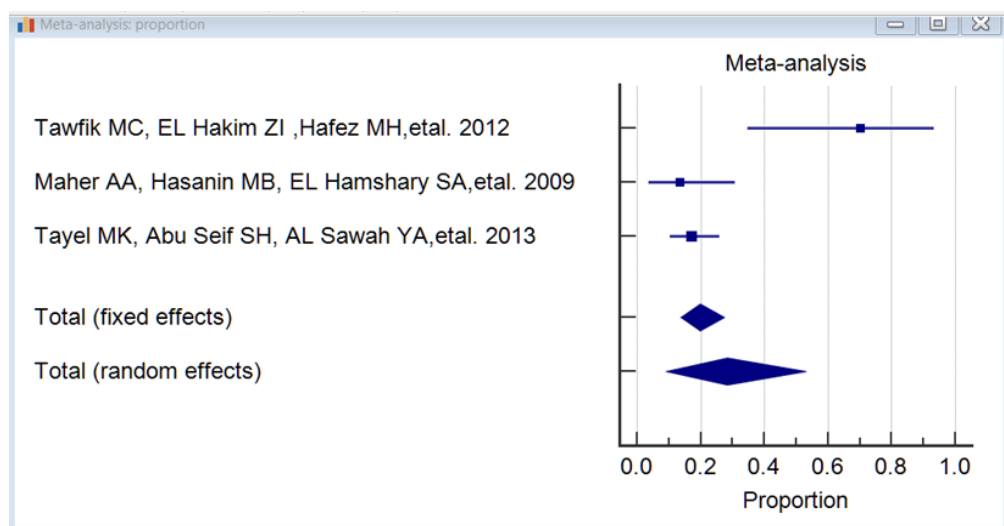
Table & Fig. 7: show cases with maternal fever, PROM and maternal UTI in jaundiced neonates with UTI in 3 studies were analyzed with total number of cases 140. The proportion was 28.23%.

**Table & Fig.(7): Meta-analysis proportion of maternal fever, PROM and maternal UTI in jaundiced cases with UTI**

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Tawfik MC, EL Hakim ZI ,Hafez MH,etal. 2012	10	70.000	34.755 to 93.326	7.69	26.57
Maher AA, Hasanin MB, EL Hamshary SA,etal. 2009	30	13.333	3.755 to 30.722	21.68	34.50
Tayel MK, Abu Seif SH, AL Sawah YA,etal. 2013	100	17.000	10.226 to 25.818	70.63	38.93
Total (fixed effects)	140	19.918	13.712 to 27.412	100.00	100.00
Total (random effects)	140	28.231	9.016 to 52.997	100.00	100.00

**Test for heterogeneity**

Q	12.5321
DF	2
Significance level	P = 0.0019
I <sup>2</sup> (inconsistency)	84.04%
95% CI for I <sup>2</sup>	52.13 to 94.68



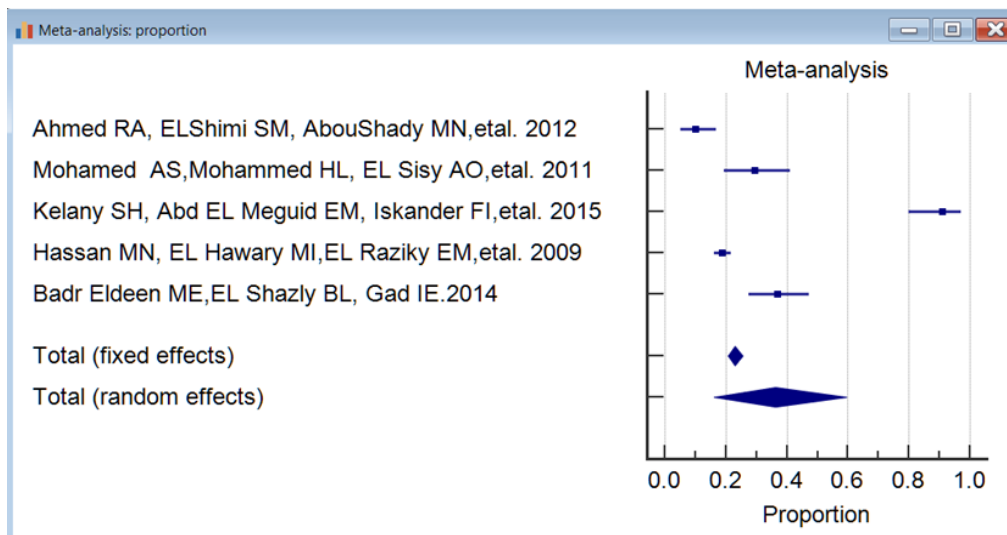


Table (4): shows cephalhematoma in cases with jaundice in 3 studies were analyzed with total number of cases 983. The proportion was 6.52%.

**Table 4: Meta-analysis proportion of cephalhematoma in jaundiced cases**

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Ahmed RA, ELShimi SM, AbouShady MN, et al. 2012	120	6.667	2.922 to 12.714	12.27	33.42
Kelany SH, Abd EL Meguid EM, Iskander FI, et al. 2015	55	14.545	6.495 to 26.663	5.68	29.20
Hassan MN, EL Hawary MI, EL Raziky EM, et al. 2009	808	1.856	1.043 to 3.043	82.05	37.38
Total (fixed effects)	983	2.847	1.901 to 4.087	100.00	100.00
Total (random effects)	983	6.526	1.259 to 15.467	100.00	100.00

Test for heterogeneity	
Q	19.6556
DF	2
Significance level	P = 0.0001
I <sup>2</sup> (inconsistency)	89.82%
95% CI for I <sup>2</sup>	72.70 to 96.21

Table (5) shows G6PD deficiency in cases with jaundice in 4 studies were analyzed with total number of cases 1083. The proportion was 4.14%.

**Table 5: Meta-analysis proportion of G6PD in jaundiced cases**

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Ahmed RA, ELShimi SM, AbouShady MN, et al. 2012	120	3.333	0.916 to 8.315	11.13	25.20
Kelany SH, Abd EL Meguid EM, Iskander FI, et al. 2015	55	7.273	2.017 to 17.587	5.15	21.84
AbuSetta KH, EL Shimi SM, ELSamahy HM, et al. 2018	100	8.000	3.517 to 15.156	9.29	24.56
Hassan MN, EL Hawary MI, EL Raziky EM, et al. 2009	808	0.495	0.135 to 1.263	74.43	28.40
Total (fixed effects)	1083	1.413	0.799 to 2.307	100.00	100.00
Total (random effects)	1083	4.141	0.673 to 10.363	100.00	100.00

Test for heterogeneity	
Q	27.8280
DF	3
Significance level	P < 0.0001
I <sup>2</sup> (inconsistency)	89.22%
95% CI for I <sup>2</sup>	75.14 to 95.33

Table (2) shows Rh incompatibility in cases with jaundice in 5 studies were analyzed with total number of cases 1158. The proportion was 16.29%.

**Table & Fig. 2: Meta-analysis proportion of Rh incompatibility in jaundiced cases**

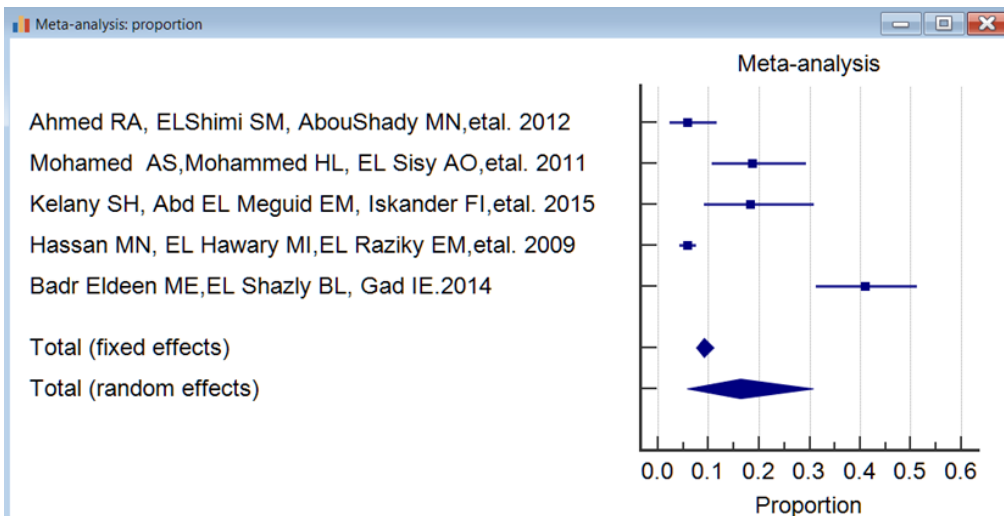
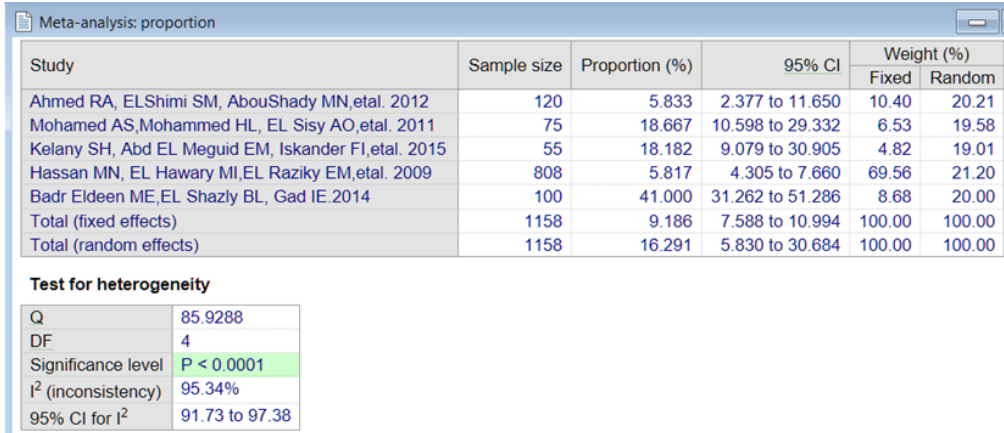
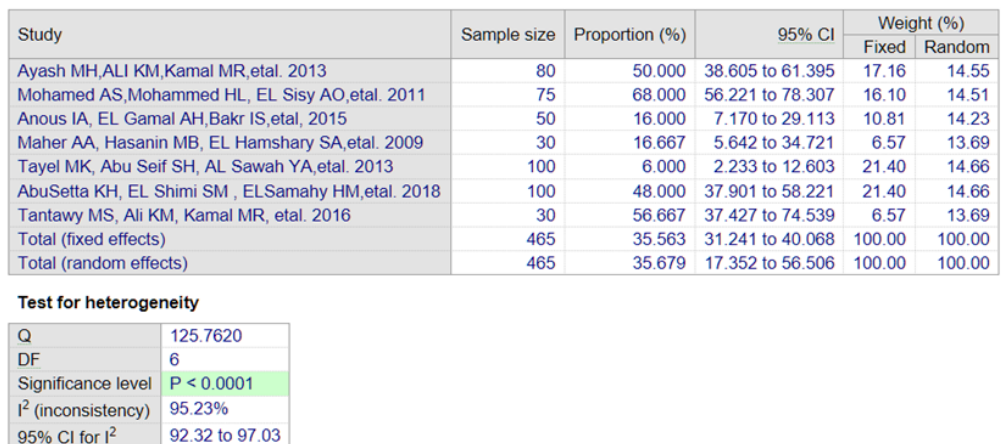


Table & Fig. 3 show ABO incompatibility in cases with jaundice in 5 studies were analyzed with total number of cases 1158. The proportion was 36.31%.

**Table & Fig. 3: Meta-analysis proportion of ABO incompatibility in jaundiced cases**



medical faculties. The researcher collected data from theses of MSc., MD., PhD which focus on neonatal jaundice in Egypt. The information was extracted from the selected studies include: first author, publication year, title of the study, type of the study design, size and characteristics of the study population.

**Inclusion criteria**

All national studies conducted on neonatal jaundice and its determinants in the period.

**Exclusion criteria**

- 1-Unreliable and irrelevant studies or studies that don't have scientific merit.
- 2-Studies with limited sample size

**Statistical analysis:**

The random effects model is assumed that the true effect size varies from one study to the next, and that the studies in our analysis represent a random sample of effect sizes that could have been observed. The goal is to estimate the mean effect in a range of studies, and we do not want that overall estimates to be overly influenced by any one of them (Higgins et al., 2003).

**MedCalc Program:**

A meta-analysis integrates the quantitative findings from separate but similar studies and provides a numerical estimate of the overall effect of interest (Petrie et al., 2003). Different weights are assigned to the different studies

for calculating the summary or pooled effect. The weighing is related with the inverse of the standard error (and therefore indirectly to the sample size) reported in the studies. Studies with smaller standard error and larger sample size are given more weight in the calculation of the pooled effect size. The effect of interest can be: an average of a continuous variable, a correlation between two variables, an odds ratio, suitable for analyzing retrospective studies, a relative risk (risk ratio) or risk difference, suitable for analyzing prospective studies, a proportion, and the area under the ROC curve. The agreement or disagreement between the studies is examined using different measures of heterogeneity. The results of the different studies, with 95% CI, and the overall effect (under the fixed and random effects model) with 95% CI are illustrated in a graph called "forest plot".

Ethical considerations:

The study proposal was approved by the local ethical committee of the Faculty of Postgraduate Childhood Studies.

**Results:**

According to guidelines by (PRISMA) statement, the researcher reviewed the Egyptian theses, papers, journals, in English language. The pool of 32 main studies involves a total sample of 3458 neonates.

Table (1) shows formula fed neonates in 7 studies were analyzed with total number of cases (465).The proportion was 35.67%.

**Table (1) Meta-analysis proportion of formula fed neonates among studied cases**

Study	Sample size	Proportion (%)	95% CI	Weight (%)	
				Fixed	Random
Ayash MH,ALI KM,Kamal MR,etal. 2013	80	50.000	38.605 to 61.395	17.16	14.55
Mohamed AS,Mohammed HL, EL Sisy AO,etal. 2011	75	68.000	56.221 to 78.307	16.10	14.51
Anous IA, EL Gamal AH,Bakr IS,etal, 2015	50	16.000	7.170 to 29.113	10.81	14.23
Maher AA, Hasanin MB, EL Hamshary SA,etal. 2009	30	16.667	5.642 to 34.721	6.57	13.69
Tayel MK, Abu Seif SH, AL Sawah YA,etal. 2013	100	6.000	2.233 to 12.603	21.40	14.66
AbuSetta KH, EL Shimi SM , ELSamahy HM,etal. 2018	100	48.000	37.901 to 58.221	21.40	14.66
Tantawy MS, Ali KM, Kamal MR, etal. 2016	30	56.667	37.427 to 74.539	6.57	13.69
Total (fixed effects)	465	35.563	31.241 to 40.068	100.00	100.00
Total (random effects)	465	35.679	17.352 to 56.506	100.00	100.00

**Test for heterogeneity**

Q	125.7620
DF	6
Significance level	P < 0.0001
I <sup>2</sup> (inconsistency)	95.23%
95% CI for I <sup>2</sup>	92.32 to 97.03

## الهدف من هذه الدراسة:

انشاء قاعدة بيانات أولية لليرقان الوليدي في مصر إضافة الي ذلك فإن الدراسة يمكن أن توفر لنا معرفة العوامل المحددة لليرقان الوليدي.

## تصميم الدراسة:

دراسة تحليل- ميتا لعينة من الدراسات المصرية والأطروحات التي تم جمعها عن طريق المكتبة الرقمية للجامعات المصرية في الفترة من ٢٠٠٥ الي 2018.

## منهجية البحث:

تم البحث من خلال المكتبة الرقمية للجامعات المصرية عن الدراسات المصرية والأطروحات المتعلقة باليرقان الوليدي في الفترة من ٢٠٠٥ الي 2018. بحث بشكل منهجي في الدراسات والأطروحات التي تناولت دراسة اليرقان الوليدي وتم ذلك باستخدام الموقع الالكتروني لإتحاد مكتبات الجامعات المصرية، جمع أكبر عدد ممكن من الأطروحات وبعد ذلك تم تقييم جودة الأطروحات باستخدام معايير موضوعية للإدراج والإقصاء، ثم تم جمع البيانات الأولية من الدراسات المختارة ثم تحليلها باستخدام التحليل البعدي (تحليل-ميتا) وهذا يعني إعادة تحليل نتائج التحليل الأولي أو الثانوي من مجموع البحوث والدراسات الفردية. بين ٣٢ دراسة شملت ٣٤٥٨ حديثي الولادة من ٢٠٠٥ إلى ٢٠١٨، تم تضمينها أخيرًا، وكانت الأسباب المجمعة لليرقان بين حديثي الولادة المصريين هي: عدم توافق ABO يمثل ٣٦,٣٪، عدم توافق Rh 16.29٪، ورم رأسي ٦,٥٢٪، ونقص G6PD 4.14٪ وأسباب أخرى ٥٥,٣٪. اليرقان الذي عولج بالعلاج الضوئي التقليدي مع ٩٦٣ حالة تمثل ٨٧,٣٤٪. اليرقان الذي عولج عن طريق نقل الدم يمثل ١٦,٦٢٪ من الحالات.

## Introduction:

Jaundice is one of the most common and annoying problems that occur in the newborn. Jaundice is observed during the first week of life in approximately 60% of term neonates and 80% of preterm neonates. Although most jaundice neonates recover without any complications, there is always a risk of unconjugated bilirubin encephalopathy during the period of hyperbilirubinemia. Because of the increasing number of early discharged newborns, there is a corresponding danger of failing to diagnose severe hyperbilirubinemia and start the treatment in time, as reports about kernicterus in full term healthy newborn demonstrate. Therefore, it is important to establish safe markers for the development of excessive jaundice in these infants (Moerschel et al., 2008).

Neonatal hyperbilirubinemia has become an important cause of readmission (Vandborg et al., 2012). Phototherapy has been known as the most effective non-invasive treatment of neonatal indirect hyperbilirubinemia (Mreihil et al., 2010).

Meta-analysis is a statistical procedure that integrates the results of numerous

independent studies; it lies on the top of evidence base medicine Hierarchy.

## Objective:

The aim of the present study is to provide the first meta-analysis of Egyptian research regarding some risk factors of neonatal jaundice among Egyptian neonates.

## Methodology:

Following the lines of preferred reporting items for systematic reviews and meta-analysis statement, the author searched data base from January 2005 to the end of December, 2018 in English language. Reviewers checked results and removed overlapping citations. Data were extracted from articles using a three-phase system. First, all articles identified through the literature were screened for eligibility criteria. We then extracted descriptive information, collecting information regarding study descriptors, participant demographic variables of the comparison group(s), diagnostic procedures, assessment measures, and summary of findings. Characteristics in each of these categories were coded. The researcher visited the libraries (central and digital) in the



## Some risk factors of Neonatal hyperbilirubinemia in Egypt (A meta-analysis study)

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### Abstract:

Background: Neonatal jaundice is a common health problem and is expected to be seen in approximately 60%–80% of healthy newborns.

**Objective:** To generate national parameters for neonatal jaundice and its determinants in Egypt. To provide the first meta-analysis of Egyptian research regarding some risk factors of neonatal jaundice among Egyptian neonates.

**Methodology:** Type of the study: Meta-analysis (type 3). We systematically searched electronic university library council data base (eulc .edu.eg) for thesis published. We included only studies that controlled for the effects of confounding variables in determining some risk factors for neonatal hyperbilirubinemia. We conducted meta-analysis of the eligible studies and computed risk estimates with random effects models. The researcher reviewed the Egyptian theses, papers, journals, in English language, searching for studies published from January 2005 to the end of December, 2018. Meta-analysis was done using MedCalc software ver. 12.7.7.0.

**Results:** Among 32 studies involving 3458 neonates from 2005 to 2018, were finally included, the overall pooled causes of jaundice among Egyptian neonates were: ABO incompatibility represented 36.3%, Rh-incompatibility 16.29%, cephalhematoma 6.52%, G6PD deficiency 4.14% and other causes 55.3%. Jaundice treated by conventional phototherapy with 963 cases represented 87.34%. Jaundice treated by exchange transfusion represented 16.62% of cases.

**Conclusion:** Phototherapy is the most continent and safe therapeutic method which is used in the first step of treatment of unconjugated neonatal jaundice. It lowers the levels of serum bilirubin and decreases the need for the potentially more invasive therapeutic approach, exchange transfusion.

**Keywords:** Meta-analysis, Neonates, Risk factors, Jaundice, Hyperbiliruminemia.

### مقدمة

اليرقان الوليدي هو اصفرار يصيب جلد وعين الطفل وهو حالة طبية تتطلب عناية خاصة بحديثي الولادة وهو ناتج عن زيادة مستوى البيليروبين في الدم عن الحد الطبيعي، والبيليروبين هي مادة تنتج عن تحلل خلايا الدم الحمراء وتكون سامة عند زيادة تركيزها في الدم، ولتجنب ذلك يقوم الكبد بالتخلص منها وطرحها في الدم، أو الأمعاء لإخراجها مع البول والبراز. يمثل اليرقان أو الصفراء في الأطفال حديثي الولادة أكثر الأمراض شيوعاً في الشهر الأول من العمر وتعد زيادة الصفراء بالدم في الأطفال حديثي الولادة (اليرقان الوليدي) مشكلة قائمة في 60% من الأطفال كاملي النمو و 80% من الأطفال المبتسرين في الأيام الثلاثة الأولى من العمر وتمثل 75% من الحالات التي يعاد حجزها بالمستشفى في خلال الأسبوع الأول من العمر. وعلى الرغم من أن العلاج النشط غير مطلوب في غالبية حالات الصفراء عند الرضع إلا أنه في بعض الأحيان قد تحدث مضاعفات خطيرة مثل الخلل في الوظائف العصبية أو الوفاة وتنقسم الصفراء إلى مرتبطة وغير مرتبطة وتنقسم الأخيرة إلى فسيولوجية ومرضية.