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RESEARCH ARTICLE

The effect of Fenofibrate and Antioxidant Vitamins [D, E and C] in Treatment of Uncomplicated Neonatal Hyperbilirubinemia.

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Abstract

Introduction: Jaundice is the most common condition that requires medical attention and hospital readmission in newborns.

Objective: To evaluate the efficacy of oral use of fenofibrate, vitamin- D and other antioxidant vitamins (E and C) in treatment of full-term neonates with indirect hyperbilirubinemia.

Patient and Methods: This is a prospective case control study carried on 80 full-term neonates suffering from unconjugated hyperbilirubinemia from January 2015 to May 2016. These neonates were randomly allocated into four groups. Group A; received only phototherapy as controls, group B received single oral dose of fenofibrate suspension in a dose 10 mg/kg beside phototherapy, group C received phototherapy and daily dose of vitamin D (400 IU/24h) and group D received phototherapy , daily dose of vitamin E (4 mg/day) and daily dose of vitamin C(40 mg/day).

Results: The mean duration of stay at hospital of fenofibrate group was 2.6±0.7 days shorter than the mean duration of stay at hospital of control group which was 5.05±0.9 days (P value = 0.001*). Vitamin D group shows mean duration of stay at hospital 2.9±0.8 days shorter than that of control group which was 5.05±0.9 days (P value =0.001*). The mean duration of stay at hospital of vitamin E & C group was 4.7±0.9 days, while mean duration of stay at hospital of control group was 5.05±0.9 days with no statistically significant difference (P value = 0.06). Conclusions: In conclusion, addition of single oral dose of fenofibrate in jaundiced baby receiving phototherapy in the first 24hours of treatment can significantly reduce the serum bilirubin levels in term newborns and duration of phototherapy.

Kay words: Antioxidant, Vitamin D, Vitamin E, Vitamin C, Neonatal, Hyperbilirubinemia.

Introduction:

Neonatal jaundice refers to the yellow coloration of the skin and sclera of newborn babies those results from the deposition of bilirubin [1]. Jaundice is the most common condition requiring medical attention in newborn babies. About 50% of term and 80% of preterm babies develop jaundice in the first week of life. Jaundice is also a common cause of re-admission to hospital after early discharge of newborn babies. Jaundice usually appears 2 to 4 days after birth and disappears 1 to 2 weeks later, usually without the need for treatment [2].

As assessed by population-based studies and registries, the incidence of severe hyperbilirubinemia in High-Income Countries (HICs) is estimated to be about 31.6/100,000 live births , while the incidences of Acute Bilirubin Encephalopathy(ABE) and kernicterus/Chronic Bilirubin Encephalopathy (CBE) have been estimated as being in the range of 1.0-3.7 and 0.4-2.7/100,000 live births, respectively [3]. On the contrary in Low- and Middle-Income Countries (LMICs) there is no harmonized protocols for hyperbilirubinemia classification and management have been implemented leading to wide variations in protocols and rendering difficult if not impossible comparisons between different locations, with the exception of Malaysia and Egypt which adopted the American Academy of Pediatrics (AAP) guidelines for neonatal jaundice (NNJ) management. Despite these limitations, the prevalence is said to be high in LMICs, where records and documentation of the incidence of NNJ, ABE and CBE are usually poor and variable [4]. The African region has the highest incidence of severe neonatal jaundice (SNJ) per 10 000 live births at 667.8, while Eastern Mediterranean at 165.7 [5].

Aim of the work: The aim of this study was to evaluate the efficacy of oral use of fenofibrate, vitamin D and other antioxidant vitamins (E and C) in the treatment of indirect neonatal hyperbilirubinemia.

Patient and Methods:

This is a prospective case control study was carried on 80 full-term neonates suffering from neonatal jaundice admitted to the Neonatal Intensive Care Unit, Minia University Hospital and Minia General Hospital from January 2015 to May 2016.

Inclusion criteria:

- Gestational age of 36 – 42 weeks.
- Indirect serum bilirubin ranges from 15 to 20 mg / dl.
- Conjugated bilirubin above 20% of total serum bilirubin or > 2 mg/dl.

- Sepsis.
- Low birth weight < 2000g.

Parental consent:

Before randomization, written parental consent was obtained for each eligible infant to participate in the study.

Study Design:

This Case control study was carried on 80 full term (FT) neonates admitted to the "NICU" Minia University Pediatric Hospital and Minia General Hospital suffering from neonatal indirect hyperbilirubinemia. These neonates were randomly allocated into four groups. we used random allocation cards using computer-generated random numbers.

The permission of their parents and the ethical committee of hospital were taken.

- All four groups received phototherapy under standard conditions. In order to minimize possible bias due to different types of phototherapy machines, we used only one type of phototherapy machine adjusted to 25 cm above the infants 'incubators. The irradiance of the phototherapy lights was monitored weekly to be maintained at 20–30 μW/cm 2 per nm with four special white 420-480 nm lamps.
- All infants were monitored continuously with a pulse oximeter (Nellcore Pleasanton, USA) and their axillary temperature was checked at 4 hours intervals. Phototherapy was ceased when indirect serum bilirubin was ≤ 12 - 13 mg/dl.
- They were fully exposed except their eyes and nappy areas.
- Breastmilk was used as can as possible together with artificial milk. The artificial milk used was full strength humanized formula given every 3 hours (8 feeds/ 24hours), the amount/feed depended on the infant's tolerance.

Group (A): included 20 neonates who received phototherapy with enteral feeding only.

Group (B): included 20 neonates who received phototherapy with enteral feeding and single oral dose of fenofibrate suspension with a dose 10 mg/kg beside phototherapy.

This study included 80 full term (FT) neonates admitted to the "NICU" of Minia University Pediatric Hospital and Minia General Hospital suffering from neonatal indirect hyperbilirubinemia, from January 2015 till May 2016. The study included 80 full term neonates (36 - 42wks): (54 males and 26 females), (45 ABO incompatibilities, 6 Rh incompatibility and 29 exaggerated physiological jaundice).

These neonates were allocated into four groups .The results are shown in tables and figures.

Control group A: Including 20 neonates (13 males & 7 females) with unconjugated hyperbilirubinemia.

All neonates in this group received only phototherapy as controls. All the neonates in this group received single oral dose of fenofibrate suspension in a dose 10 mg/kg beside phototherapy. All the neonates in this group received phototherapy and daily dose of vitamin D (400 IU / 24h) . All the neonates in this group received phototherapy , daily dose of vitamin E (4 mg / day) and daily dose of vitamin C (40 mg /day). Group B: Including 20 neonates (14 males & 6 females) with unconjugated hyperbilirubinemia. All the neonates in this group received single oral dose of fenofibrate suspension in a dose 10 mg/kg beside phototherapy. All the neonates in this group received phototherapy and daily dose of vitamin D (400 IU / 24h). All the neonates in this group received phototherapy, daily dose of vitamin E (4 mg / day) and daily dose of vitamin C (40 mg /day). Group C: Including 20 neonates (13 males & 7 females) with unconjugated hyperbilirubinemia.

All the neonates in this group received phototherapy and daily dose of vitamin D (400 IU / 24h). All the neonates in this group received phototherapy, daily dose of vitamin E (4 mg / day) and daily dose of vitamin C (40 mg /day) . Group D: Including 20 neonates (14 males & 6 females) with unconjugated hyperbilirubinemia. All the neonates in this group received phototherapy, daily dose of vitamin E (4 mg / day) and daily dose of vitamin C (40 mg /day).

Both of bilirubin levels as well as the days of staying in hospital were compared between the different study groups.

Results:

There were no significant statistical differences between the studied groups as regard sex, age on admission, gestational age, mode of delivery, blood groups and weight (Table 1). The mean duration of stay at hospital of fenofibrate group was 2.6±0.7 days shorter than the mean duration of stay at hospital of control group which was 5.05±0.9 days with significant P value = 0.001*(Table 2). Vitamin D group shows mean duration of stay at hospital 2.9±0.8 days shorter than that of control group which was 5.05±0.9 days with significant P value =0.001*(Table 3). The mean duration of stay at hospital of vitamin E & C group was 4.7±0.9 days, while mean

duration of stay at hospital of control group was 5.05±0.9 days with no statistically significant difference (P value = 0.06) (Table 4). The serum levels of indirect bilirubin in fenofibrate group at 24th,48th and 72th hours after starting the treatment were significantly lower than those in control group (P value = 0.001) for each of them and the duration of treatment in control group was longer than fenofibrate group (Table 5). The serum levels of indirect bilirubin in vitamin D group at 24th,48th and 72th hours after starting the treatment were significantly lower than those in control group (P value = 0.001) (Table 6). The serum levels of indirect bilirubin in vitamin C&E group at 24th,48th and 72th hours after starting the treatment showed non-significant differences with levels of control group p values were 0.3, 0.4 and 0.5 respectively (Table 7). The mean duration of phototherapy needed in fenofibrate group was the shortest followed by vitamin D group and then vitamin C&E group.(Table 8)

Discussion:

Neonatal jaundice (NNJ), is usually benign, but in some cases it can progress to severe hyperbilirubinemia, acute bilirubin encephalopathy (ABE) and kernicterus/chronic bilirubin encephalopathy (CBE). ABE and CBE are largely preventable if severe hyperbilirubinemia is identified early and treated promptly [6]. Guidelines for managing jaundice have been proposed by the American Academy of Pediatrics (AAP), the UK National Institute for Health and Care Excellence (NICE) and others [7-8].Although timely use of high performance phototherapy devices has been established in the effective management of neonatal hyperbilirubinemia (NHB), the condition still remains a leading cause of morbidity and mortality in resource-constrained settings [9].

The aim of this study was to compare between the effect of phototherapy alone and phototherapy together with oral fenofibrate, vitamin D or vitamin C&E on indirect serum bilirubin level in neonates with hyperbilirubinemia to decrease the duration of stay at NICU.

This study was performed in Minia Neonatal Intensive Care unit, from January 2015 till May 2016. The study included 80 full term neonates (36-42wks) suffering from neonatal

hyperbilirubinemia who were divided into four groups: Group (A) which included 20 neonates who received phototherapy with enteral feeding only , Group (B) which included 20 neonates who received phototherapy with enteral feeding and single oral dose of fenofibrate , Group (C) which included 20 neonates who received phototherapy with enteral feeding and daily dose of vitamin D and Group (D) which included 20 neonates who received phototherapy with enteral feeding and daily dose of vitamin C& vitamin E .The mean age of the neonates on admission to our NICU was (3.2±1.3) days in Group (A), in Group (B) was (3.3±1.5) days , in Group C (3.1±1.2) and in Group (D) was (3.1±1.1) with no significant difference between the four groups (table 1).This is because the typical course of physiologic jaundice peaks around days two to four with or without another cause of jaundice such as RH or ABO incompatibility [10] explained that Jaundice occurs when there is accumulation of bilirubin in the skin and mucous membranes. In most infants with jaundice there is no underlying disease, and the jaundice is termed physiological. Physiological jaundice typically presents on the second or third day of life and results from the increased production of bilirubin (owing to increased circulating red cell mass and a shortened red cell lifespan) and the decreased excretion of bilirubin (owing to low concentrations of the hepatocyte binding protein, low activity of glucuronosyl transferase, and increased enterohepatic circulation) that normally occur in newborn babies [11].

In the current study males present > 60 % of the cases in four groups. This was in agreement with several reports demonstrate that males neonates have higher serum levels of indirect bilirubin than females neonates [12] and also in agreement with Al-Asy et al 2015 [13] where males neonates presents 65 % of cases. Although causes are unknown this may be explained by many factors. Tioseco et al. [14] described an association between males fetus pregnancies and dysfunction of the placenta which can be a factor. In addition, a higher metabolic rate in the males fetuses may be another contributing factor. This theory is enforced by the fact that XY blastocysts and embryos grow at an accelerated rate when compared with XX chromosome bearers [13].

In our study, there was a statistically significant difference between fenofibrate group and control group as regard the duration for phototherapy. The mean duration of stay at hospital of fenofibrate group was 2.6±0.7 days, while mean duration of stay at hospital of control group was 5.05±0.9 days with

significant P value = 0.001* (Table 2). Also babies in fenofibrate group showed lower values in the mean of successive serum levels of indirect bilirubin in comparison with the control group. (Table 6)

This study showed the response of babies to decrease the level of indirect bilirubin and our results is coincident with the findings of Kumar et al.,2012 where all neonates in fenofibrate group , after 48 hours of starting the treatment did not need phototherapy while in contol group25% of neonates admitted for 96 hours (P= <0.001) [13].This can be explained by that Fenofibrate induce bilirubin conjugation via induction of glucuronyl transferase activity and converts unconjugated bilirubin to conjugated bilirubin, so it increases its clearance by making bilirubin soluble and thus fit for renal excretion [15]. Fenofibrate produces some side effects in adults as gastrointestinal upset and muscle cramps with prolonged use but in neonatal period in a single dose it causes no side effects in our study and up to one month after therapy [16]. Also in our study, there was a statistically significant difference between vitamin D group and control group in the duration of phototherapy at hospital. vitamin D group shows mean duration of stay at hospital 2.9±0.8 days shorter than that of control group which was 5.05±0.9 days with significant P value =0.001* (table 3). We found that babies in vitamin D group showed lower values in successive serum indirect bilirubin levels (table 7). This is explained by that active form of vitamin D,(1,25 dihydroxy vitamin D3) induces vitamin D receptors (VDR) which in turn act as a receoptor for secondary bile acids, such as lithocholic acid and 3-ketocholanic acid , and results in their catabolism via induction of cytochrom (CYP) 3A enzymes [17]. Vitamin D receptor (VDR) is activated by natural ligands, 1α, 25-dihydroxy-vitamin D_3 [1α,25$(OH)_2$-D_3] and lithocholic acid [18]. Also Vitamin D was shown to regulate bile acid metabolism and transport and repress the cholestasis induced inflammatory response [19].

These results are supported by studies showed that deficiency of vitamin D is associated with increased incidence of jaundice in full neonates. For example, some studies showed results suggested that low level of serum vitamin D may associate with hyper-bilirubinaemia in full-term neonates [20-22].

Also another studies done by Altayeb et al., 2016 [23] where newborn vitamin D levels were significantly lower in jaundiced cases compared with those in the non-jaundiced healthy groups, which may reveal an association between indirect hyperbilirubinemia and serum vitamin D levels.

On the other hand, Belvisi et al., 2016 [24] found that increased oxidative stress in neonatal jaundice babies leads to decrease in the levels of antioxidants like GSH and ascorbic acid and disturb their metabolism, that weaken their ability to fight the growing stress. Intense oxidative stress and decreased antioxidants may contribute to neural cell death and alter the erythrocyte membrane structure processing in neonatal jaundice.

So, giving daily dose of vitamin C and vitamin E in jaundiced neonates may lower the level of indirect bilirubin and decrease the duration needed for phototherapy but this did not happened. There was no statistically significant difference between vitamin C&E group vs. control group. The mean duration of stay at hospital of vitamin E & C group was 4.7±0.9 days, while mean duration of stay at hospital of control group was 5.05±0.9 days with non-significant P value = 0.02 (table 4) and no significant difference as regard the response of babies to decrease the level of indirect bilirubin.

This can be explained by that, in term infants, antioxidant defenses are sufficiently present at birth to counteract the hyperoxic challenge, because antioxidant enzymes mature during late gestation. Several weeks before birth, parallel with the rapid rise in lung surfactant, there is a 150 to 200% increase in SOD and glutathione peroxidase. In addition, the transfer of several antioxidants across the placenta increases during the last days of pregnancy [24].

Also Muto et al., 2015 [25] stated that supplemental vitamin E did not prevent cholestasis. Additional vitamin E was not associated with reduced inflammation or oxidative stress.

Another study by Mirzarahimi et al.,2016 [26] showed that there was no any significant relationship between the levels of bilirubin, serum uric acid, vitamin A, C, E, catalase and Glutathione, but honestly we must say that Fenofibrate produces some side effects in adults as gastrointestinal upset and muscle cramps with prolonged use but in neonatal period in a single dose it causes no side effects in our study and up to one month after therapy. According to the results of this study, we can recommend the use of a single oral dose of fenofibrate (with a dose 10 mg/kg) with phototherapy accelerates bilirubin conjugation and excretion via induction of glucuronyl transferase activity hence reduces the duration of stay at hospital. Furthermore, fenofibrate decreases the cost of stay, lowers the cost/benefit ratio and at the same time fenofibrate is safe and economic. Although, no side - effects of fenofibrates were observed after a single dose, further studies with a more precise and longer follow up is needed

for proving its safety to be used in the treatment of neonatal hyperbilirubinemia. Further studies is needed using active form of vitamin D (1, 25-dihydroxy vitamin D3[1,25(OH)2D3]) during phototherapy of uncomplicated jaundice, as the use of daily dose of vitamin D (400 IU / 24h) (non-active) with phototherapy reduces the duration of stay in hospital as vitamin D induces vitamin D receptors (VDR) which in turn act as a receptor for secondary bile acids. Furthermore, vitamin D has antineoplastic effects that act as prophylaxis against the possible carcinogenic hazardous of phototherapy. Further studies with a more precise and higher therapeutic doses of vitamin C and E is needed for proving the effect of them to be used in the treatment of neonatal hyperbilirubinemia. Finally, further studies are needed using these agents (fenofibrate, vitamin D and vitamin E&C) in treatment of uncomplicated jaundice with lower serum levels of indirect bilirubin (not risk) without phototherapy with follow up of serum indirect bilirubin at shorter intervals each 6-12h to determine its efficacy in dispensing phototherapy.

Conclusion:

In conclusion, addition of single oral dose of fenofibrate in jaundiced baby receiving phototherapy in first 24h of treatment can significantly reduce the serum bilirubin levels in term newborns and duration of phototherapy .

Giving daily therapeutic dose of vitamin D in jaundiced baby under phototherapy can significantly reduce the serum levels of indirect bilirubin in term newborns, decrease the duration of phototherapy and act as prophylaxis against hazards of phototherapy.

Conflict of interest: The authors declared no conflict of interest.

Author's contributions: SS and SN conceived the study. NZ revised the patients' medical reports and the final manuscript. All authores revised the final draft of the manuscript.

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References:

1. Abbaspour, N., Hurrell, R. & Kelishadi, R.. Review on iron and its importance for human health. Journal Of Research In Medical Sciences: The Official Journal Of Isfahan University Of

Medical Sciences 2014; 19 (2) : 164-174.

2. Ayyappan, S., Philip, S., Bharathy, N., Ramesh, V., Kumar, C. N., Swathi, S. & Kumar, A. A. Antioxidant status in neonatal jaundice before and after phototherapy. Journal of pharmacy & bioallied sciences 2015; 7(suppl 1): s16-s21.
3. Bikle, D. Vitamin D metabolism, mechanism of action, and clinical applications. Chemistry & biology 2014; 21 (3) : 319-329.
4. American Academy of Pediatrics Steering Committee on Quality Improvement and Management., Classifying recommendations for clinical practice guidelines. Pediatrics. 2004 Sep;114(3):874-7.
5. Dennery, P. A. Pharmacological interventions for the treatment of neonatal jaundice. Seminars in neonatology 2002; 7 (2) :111 -119.
6. Gallagher, P. G. Abnormalities of the erythrocyte membrane. Pediatric clinics of North America 2013; 60 (6):1349-1362.
7. Haussler, M. R., Whitfield, G. K., Kaneko, I., Haussler, C. A., Hsieh, D., Hsieh, J.-C. & Jurutka, P. W. Molecular mechanisms of vitamin D action. Calcified tissue international 2013; 92 (2): 77-98.
8. Koekkoek, W. & Van Zanten, A. R.. Antioxidant vitamins and trace elements in critical illness. Nutrition in clinical practice 2016; 31(4): 457-474.
9. Maisels, M. J., Newman, T. B., Stevenson, D. & Watchko, J. Care of The Jaundiced Neonate, New York: Mcgraw-Hill 2012; .ch5: 66 -86.
10. Mreihil, K., Benth Jūratė, Š. Stensvold Hans, J., Nakstad, B. & Hansen Thor Willy, R.. Phototherapy is commonly used for neonatal jaundice but greater control is needed to avoid toxicity in the most vulnerable infants. Acta Paediatrica 2017; 107 (4): 611-619.
11. Greco, C., Arnolda, G., Boo, N. Y., Iskander, I. F., Okolo, A. A., Rohsiswatmo, R., Shapiro, S. M., Watchko, J., Wennberg, R. P., Tiribelli, C. & Coda Zabetta, C. D.. Neonatal jaundice in low- and middle-income countries: lessons and future directions from the 2015 don ostrow trieste yellow retreat. Neonatology 2016; 110 (3): 172-180.
12. . Neonatology 2016; 110 (3) : 172-180.

13. Cline, B. K., Vreman, H. J., Faber, K., Lou, H., Donaldson, K. M., Amuabunosi, E., Ofovwe, G., Bhutani, V. K., Olusanya, B. O. & Slusher, T. M.. Phototherapy device effectiveness in Nigeria: irradiance assessment and potential for improvement. Journal of tropical pediatrics 2013; 59 (4) : 321-325.
14. Mreihil, K., Benth Jūratė, Š., Stensvold Hans, J., Nakstad, B. & Hansen Thor Willy, R.. Phototherapy is commonly used for neonatal jaundice but greater control is needed to avoid toxicity in the most vulnerable infants. Acta Paediatrica 2017; 107 (4) : 611-619.
15. Woodgate, P. & Jardine, L. A.. Neonatal jaundice: phototherapy. BMJ Clinical Evidence 2015; 2015 : 0319.
16. Stevenson, D. K., Maisels, M. J. & Watchko, J. F.. Care of the jaundiced neonate, Mcgraw-Hill Medical New York 2012; ch10:195-220.
17. Tioseco, J. A., Aly, H., Milner, J., Patel, K. & El-Mohandes, A. A.. Does gender affect neonatal hyperbilirubinemia in low-birth-weight infants? Pediatric Critical Care Medicine 2005; 6 (2) : 171-174.
18. Kumar, B., Agarwal, P., Chorishi, A. & Dhaneria, M.. Fenofibrate: a novel approach in treating uncomplicated neonatal hyperbilirubinemia. People's Journal of Scientific Research2012; 5 (2): 5-8
19. Al-Asy, H. M., El-Sharkawy, H. M., Mabrouk, M. M. & Hamad, M. R.. Effect of fenofibrate on indirect neonatal hyperbilirubinemia. Journal of clinical neonatology 2015; 4(2) : 82 - 86.
20. Asemi, Z., Karamali, M. & Esmaillzadeh, A.. Favorable Effects of Vitamin D Supplementation on Pregnancy Outcomes in Gestational Diabetes: A Double Blind Randomized Controlled Clinical Trial. Hormone and Metabolic Research 2014; 47(08): 565-570.
21. Han, S., Li, T., Ellis, E., Strom, S. & Chiang, J. Y. L.. A novel bile acid-activated vitamin D receptor signaling in human hepatocytes. Molecular endocrinology 2010; 24 (6) : 1151-1164.
22. Guo, G. Y., Shi, Y. Q., Wang, L., Ren, X., Han, Z. Y., Guo, C. C., Cui, L. N., Wang, J. B., Zhu, J. & Wang, N.. Serum vitamin D level is associated with disease severity and response to ursodeoxycholic acid in primary biliary

cirrhosis. Alimentary pharmacology & therapeutics 2015; 42 (2) : 221-230.

23. Mutlu, M., Çayir, A., Çayir, Y., Özkan, B. & Aslan, Y.. Vitamin D and hyperbilirubinaemia in neonates. Hk J paediatr (new series) 2013; 18 (2) : 77-81.
24. Aletayeb, S. M. H., Dehdashtiyan, M., Aminzadeh, M., Malekyan, A. & Jafrasteh, S.. Comparison between maternal and neonatal serum vitamin D levels in term jaundiced and nonjaundiced cases. Journal of the chinese medical association 2016; 79 (11) : 614-617.
25. Belvisi, E., Bracciali, C., Ognean, M. L., Tei, M., Negro, S., Carra, F., Proietti, F., Buonocore, G. & Perrone, S.. Enzyme activities in erythrocytes of term and preterm newborns. Journal of pediatric biochemistry 2016 ; 6 (2) :114-117.
26. Muto, M., Lim, D., Soukvilay, A., Field, C., Wizzard, P. R., Goruk, S., Ball, R. O., Pencharz, P. B., Mi, S., Curtis, J., Wales, P. W. & Turner, J. M.. Supplemental parenteral vitamin E into conventional soybean lipid emulsion does not prevent parenteral nutrition–associated liver disease in full-term neonatal piglets. Journal of parenteral and enteral nutrition 2015; 41 (4) : 575-582.
27. Mirzarahimi, M., Ahadi, A., Bohlooli, S., Namakikhalajan, E. & Barak, M.. Antioxidant levels in cord blood of term neonates and its association with birth weight. Iranian journal of child neurology 2016; 10 (1) : 31-48.

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