

**How to Cite:**

Alomda, F. A. A., Diab, Y. M. S., & Ahmed, K. I. S. (2022). Evaluation of transdermal nitroglycerine as tocolytic agent in preterm labour. *International Journal of Health Sciences*, 6(S4), 2963–2972. <https://doi.org/10.53730/ijhs.v6nS4.9677>

## Evaluation of transdermal nitroglycerine as tocolytic agent in preterm labour

**Fahd Abd Alaal Alomda**

Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Egypt

**Yasser Muhammed Saeed Diab**

Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Egypt

**Khaled Ibrahim Sultan Ahmed**

Obstetrics and Gynecology department, Faculty of Medicine, Al-Azhar University, Egypt

Corresponding author email: [Kaled.soltan123456@gmail.com](mailto:Kaled.soltan123456@gmail.com)

**Abstract---**Background: Preterm birth continues to be a problem for obstetricians. Preterm birth complicates 8-10% of birth. Although the causes of preterm labor are not well understood, the burden of preterm birth is clear. Aim and objectives: The aim was to study to evaluate the efficacy and safety of transdermal nitroglycerin as tocolytic agent in women with preterm labor. Subjects and methods: This prospective randomized controlled trial was conducted in obstetrics and Gynecology department, AL- HUSSEIN University Hospital. The study was carried out on total of 100 patients with preterm labour. They were randomly assigned to either the nitroglycerine patch or bed rest alone. The duration of the study ranged from 6- 12 months. Results: out of 50 women in the TNG group, a total of 47 (94.0%) women benefited from the GTN patch and the labor pains stopped within the first few hours. Only 3 (6.0%) patients could not go beyond 48 hours. Delivery was deferred for 48 to less than 72 hours, 72 to <96 hours, 96 to < 7days and more than 7 days in 4(8.0%), 11(22.0%), 4(8.0%) and 28(56.0%) respectively. Conclusion: TNG appear to be at least as effective as the commonly used tocolytics today. NTG patch may prove to be the drug of choice for acute uterine relaxation in cases of preterm labour.

**Keywords---**nitroglycerine, preterm labour, ritodrine.

## Introduction

Preterm labour (PTL) is defined as the onset of labour after the age of viability (20–24 weeks) and before 37 completed weeks of pregnancy. <sup>1</sup> While the exact mechanism of preterm labour remains unclear, it is most frequently associated with either a pathology causing uterine contractions or early/untimely initialization of normal physiological uterine contractions, leading to preterm deliveries. <sup>2</sup> Preterm represents a serious public health problem in 7-12% of the pregnancies and results in up to 70-80% of neonatal morbidity and mortality. <sup>3</sup> Practically, survival outcomes are better in births after 34 weeks of gestation, because of rapid advancements in fetomaternal medicine during the last few years. <sup>2</sup>

The major neonatal morbidity includes respiratory distress syndrome, intraventricular hemorrhage. Patent ductus arteriosus, sepsis, necrotizing, enterocolitis, periventricular leukomalacia and retinopathy of prematurity. <sup>4</sup> On the long-term basis, the preterm infants are found to be more at risk for neurodevelopmental handicaps like cerebral palsy, hearing loss, and blindness. Also, a wide spectrum of intellectual impairments may be present. The non-neurologic long-term sequelae can be chronic pulmonary disease or the compromise in overall growth of the preterm baby. <sup>5</sup> Tocolytic therapy continues to be the focus of treatment of preterm labor to allow the administration of antenatal corticosteroids for improving fetal lung maturity and to transfer the mother to a tertiary care facility with a neonatal intensive care unit. <sup>6</sup>

Nitroglycerine is a drug with a high first pass inactivation in liver. The active substance is rapidly metabolized in the liver by a glutathione dependent organic nitrate reductase. <sup>7</sup> To avoid it, transdermal use of the drug is beneficial. In transdermal drug administration the drug is delivered at a constant and predictable rate, so a smooth plasma concentration of the drug is reached without fluctuations. <sup>8</sup> The study aimed to evaluate the efficacy and safety of transdermal nitroglycerin as tocolytic agent in women with preterm labor.

## Patients and Methods

A prospective randomized controlled trial conducted in Obstetrics and Gynecology department, AL- HUSSEIN University Hospital. The study was carried out on total of 100 patients with preterm labour. They were randomly assigned to either the nitroglycerine patch or bed rest alone, only the staff will know which of the patients is using either regimen.

Ethical consideration: the protocol was considered official after the acceptance by ethical committee of the faculty.

Inclusion Criteria: Gestational age between 28 to 34 wks as determined by menstrual dates, clinical examination, USG, uterine contractions: 2 contractions in 10-minute period, each contraction lasting for 40 sec, progressive cervical effacement 80% or greater, cervical dilatation up to 3 cm and intact membranes

Exclusion Criteria: Maternal Factors: Rupture of Membrane, infection, cervical dilatation greater than 3 cm, antepartum hemorrhage, pregnancy induced hypertension, chronic hypertension, cardiac disease, previous caesarean section,

renal disease and pulmonary disorder – Asthmatics, ARDS. Fetal Factors: Multiple gestations, fetal death / distress, IUGR, congenital anomalies, polyhydramnios / Oligohydramnios and erythroblastosis

## Methods

All patients was subjected to;

History taking: Personal date: (Name, age, sex, address, phone number, occupation). Menstrual history Past history

Investigation: Urine analysis, Complete Blood count, vaginal swab and ultrasound

Drug protocol: Group A: Patients was received Transdermal Nitroglycerine patch (NTG -10) releasing nitroglycerine at the rate of 10 mg per 24 hours which is applied on the anterior abdominal wall. If no change in contractions occurs or there is an increase in intensity, frequency or duration of contractions after one hour of placement of first NTG Patch, one additional NTG Patch of same dose was applied, and then both patches were continued for 24 hours. Treatment discontinued if: BP falls < 90 / 60 mm Hg, PR > 100 / min, Patient had PROM and Uterine contractions persist for > 24 hours even after applying 20 mg of Nitroglycerine patch. Group B: Observed with bed rest.

Both Group A and B: 2 doses of Betamethasone 12 mg IM 24 hours apart are given.

Maternal outcome: Successful tocolysis (uterine contraction subside and tocolysis achieve for > 48 hours, duration of prolongation of pregnancy, completion of course of maternal steroids, gestational age at delivery, mode of delivery and adverse drug reactions.

Fetal outcomes: NICU admission and neonatal death

## Statistical analysis

Analysis of data was done using SPSS (statistical package for social science version 20 as follows: Description of quantitative variables as mean, SD and range. Description of qualitative variables as number and percentage. Chi-square test was used to compare qualitative variables between groups. Fisher exact test was used instead of chi-square when one expected less than or equal 5. T-test was used to compare quantitative variables, in parametric data (SD<50% mean). The relative risk (RR), Risk difference (RD), and odds ratio (OR). The 95% confidence interval (CI) is used to estimate the precision of the OR. Risk Difference (RD), Mean difference, the 95% confidence interval (CI).

## Results

Table (1): Demographic characteristics of the studied groups (n=100)

|                    | TNG group<br>(n=50) | Placebo<br>group (n=50) | P-value# |
|--------------------|---------------------|-------------------------|----------|
| Age                |                     |                         |          |
| • Mean $\pm$ SD    | 28.88 $\pm$ 6.38    | 27.60 $\pm$ 5.73        | 0.29T    |
| • Range            | (18-42)             | (18-39)                 |          |
| Parity No. (%)     |                     |                         |          |
| • 0 (primigravida) | 9(18.0)             | 12(24.0)                | 0.50     |

|                                                                                                                            |                                           |                                          |      |
|----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|------------------------------------------|------|
| <ul style="list-style-type: none"> <li>• 1</li> <li>• 2</li> <li>• <math>\geq 3</math></li> </ul>                          | 8(16.0)<br>10(20.0)<br>23(46.0)           | 8(16.0)<br>14(28.0)<br>16(32.0)          |      |
| History of pre-term labor No. (%)                                                                                          |                                           |                                          |      |
| <ul style="list-style-type: none"> <li>• Present</li> <li>• Absent</li> </ul>                                              | 5(10.0)<br>45(90.0)                       | 2(4.0)<br>48(96.0)                       | 0.44 |
| History of abortion No. (%)                                                                                                |                                           |                                          |      |
| <ul style="list-style-type: none"> <li>• Present</li> <li>• Absent</li> </ul>                                              | 23(46.0)<br>27(54.0)                      | 20(40.0)<br>30(60.0)                     | 0.55 |
| Gestational age at delivery (week) No. (%)                                                                                 |                                           |                                          |      |
| <ul style="list-style-type: none"> <li>• <math>&gt;37</math></li> <li>• 35-37</li> <li>• 33-34</li> <li>• 29-32</li> </ul> | 2(4.0)<br>10(20.0)<br>6(12.0)<br>32(64.0) | 0(0.0)<br>8(16.7)<br>9(18.8)<br>31(64.6) | 0.54 |
| Completion of course of maternal steroids ( $<34$ weeks) No. (%)                                                           | 34 out of 38<br>(89.5)                    | 33 out of 42<br>(78.6)                   | 0.19 |

# Chi-square test was used

T t-test was used

In the TNG group the mean age of women was  $28.88 \pm 6.38$  greater than the mean age of women in the other group  $27.60 \pm 5.73$ . Preterm labor was more in multiparous women 41(82%) in TNG group and 38(76%) in the other group with no statistically significant difference between both groups ( $p$  value  $> 0.05$ ). Table (1)

Table (2): Laboratory investigations of the studied groups (n=100)

|                                                                                               | TNG group<br>(n=50)                         | Placebo group<br>(n=50)                      | P-<br>value# |
|-----------------------------------------------------------------------------------------------|---------------------------------------------|----------------------------------------------|--------------|
| RH No. (%)                                                                                    |                                             |                                              |              |
| <ul style="list-style-type: none"> <li>• Positive</li> <li>• Negative</li> </ul>              | 20(40.0)<br>30(60.0)                        | 28(56.0)<br>22(44.0)                         | 0.11         |
| ABO group No. (%)                                                                             |                                             |                                              |              |
| <ul style="list-style-type: none"> <li>• A</li> <li>• B</li> <li>• AB</li> <li>• O</li> </ul> | 12(24.0)<br>14(28.0)<br>7(14.0)<br>17(34.0) | 11(22.0)<br>13(26.0)<br>14(28.0)<br>12(24.0) | 0.35         |
| Vaginal culture No. (%)                                                                       |                                             |                                              |              |
| <ul style="list-style-type: none"> <li>• Positive</li> <li>• Negative</li> </ul>              | 3(6.0)<br>47(94.0)                          | 5(10.0)<br>45(90.0)                          | 0.72         |
| Urine culture No. (%)                                                                         |                                             |                                              |              |
| <ul style="list-style-type: none"> <li>• Positive</li> <li>• Negative</li> </ul>              | 5(10.0)<br>45(90.0)                         | 4(8.0)<br>46(92.0)                           | 1.00         |
| Urea(mg/dl)                                                                                   |                                             |                                              |              |
| <ul style="list-style-type: none"> <li>• Mean <math>\pm</math>SD</li> <li>• Range</li> </ul>  | 29.96 $\pm$ 9.08<br>15.0-44.3               | 27.86 $\pm$ 8.17<br>15.8-42.0                | 0.23 T       |
| Creatinine (mg/dl)                                                                            |                                             |                                              |              |

|                    |                  |                  |        |
|--------------------|------------------|------------------|--------|
| • Mean $\pm$ SD    | 0.81 $\pm$ 0.15  | 0.80 $\pm$ 0.14  | 0.79 T |
| • Range            | 0.6-1.0          | 0.6-1.0          |        |
| Hemoglobin (gm/dl) |                  |                  |        |
| • Mean $\pm$ SD    | 11.87 $\pm$ 0.96 | 11.83 $\pm$ 0.97 | 0.84 T |
| • Range            | 10.2-13.3        | 10.3-13.3        |        |

# Chi-square test was used

T t-test was used

Regarding laboratory investigations of the studied groups, the results of the study revealed that, 20(40.0%) of women in the TNG group were RH positive 12(24.0%) were blood group A , 14(28.0%) were B group, 7(14.0%) were AB group and 17(34.0%) were O group. On the other group hand, 28(56.0%) of women in the TNG group were RH positive, 11(22.0%) were blood group A, 13(26.0%) were B group, 14(28.0%) were AB group and 12(24.0%) were O group, with no statistically significant difference between both groups (p value>0.05). Table (2)

Table (3): Outcome of TNG in the studied group (n=50)

|                                              | TNG group<br>(n=50) |
|----------------------------------------------|---------------------|
| Success of tocolysis No. (%)                 |                     |
| • Succeed                                    | 47(94.0)            |
| • Failed                                     | 3(6.0)              |
| Duration of prolongation of delivery No. (%) |                     |
| • <48 hours                                  | 3(6.0)              |
| • 48-<72 hours                               | 4(8.0)              |
| • 72-<96 hours                               | 11(22.0)            |
| • 96hours-<7 days                            | 4(8.0)              |
| • $\geq$ 7 days                              | 28(56.0)            |
| Side effects of TNG No. (%)                  |                     |
| • Headache                                   | 8(16.0)             |
| • Hypotension                                | 4(8.0)              |
| • Vomiting                                   | 3(6.0)              |
| • Irritation at patch site                   | 3(6.0)              |
| • No side effect                             | 32(64.0)            |

The results of the study revealed that out of 50 women in the TNG group, a total of 47 (94.0%) women benefited from the GTN patch and the labor pains stopped within the first few hours. Only 3 (6.0%) patients could not go beyond 48 hours. Delivery was deferred for 48 to less than 72 hours, 72 to <96 hours, 96 to < 7days and more than 7 days in 4(8.0%), 11(22.0%), 4(8.0%) and 28(56.0%) respectively. Table (3) and figure (1)

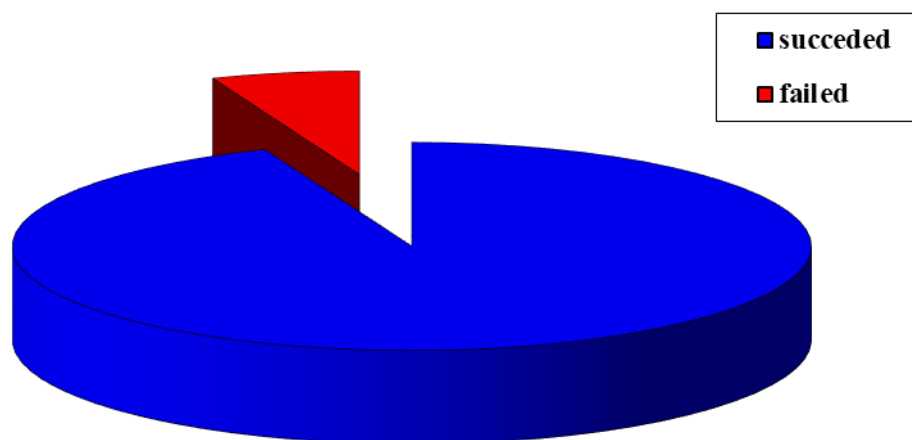


Figure (1).Frequency of success of TNG as tocolytic agent among studied group

Table (4): Neonatal outcomes of the studied group (n=100)

|                                            | TNG group<br>(n=50) | Placebo group<br>(n=50) | P-<br>value# |
|--------------------------------------------|---------------------|-------------------------|--------------|
| Birth weight at birth (kg) No. (%)         |                     |                         |              |
| • ≤1.8                                     | 5(10.0)             | 8(16.0)                 | 0.00*        |
| • 1.9-2.1                                  | 7(14.0)             | 17(34.0)                |              |
| • 2.2-2.4                                  | 18(36.0)            | 17(34.0)                |              |
| • >2.4                                     | 20(40.0)            | 8(16.0)                 |              |
| Apgar score <7 at 5 min. No. (%)           | 3(6.0)              | 11(22.0)                | 0.02*        |
| Required Resuscitation No. (%)             | 3(6.0)              | 11(22.0)                | 0.02*        |
| Respiratory Distress Syndrome RDS) No. (%) | 2(4.0)              | 7(14.0)                 | 0.16         |
| NICU admission No. (%)                     | 3(6.0)              | 6(12.0)                 | 0.49         |
| Required Mechanical Ventilation No. (%)    | 3(6.0)              | 6(12.0)                 | 0.49         |
| Death No. (%)                              | 3(6.0)              | 8(16.0)                 | 0.11         |

# Chi-square test was used

\*statistically significant at 95% level of confidence

Regarding the neonatal outcomes, the results of the study showed that all the (100%) babies were born alive. Birth weight of more than 2.4 kg was noted in 20 (40.0%), while 18 (36.0%) were born with birth weight between 2.2 to 2.4kg, 7 (14.0%) babies had weight of 1.9kg to 2.1kg and only 5 (10.0%) had weight of less than 1.8kg in the TNG group as compared to 8(16.0%), 17(34.0%), 17(34.0%) and 8(16.0%) respectively in the other group with statistically significant difference between both groups (p value<0.05). In TNG group 3(6.0%) neonates had Apgar Score <7 at 5 minutes and thus required resuscitation while in the placebo group 11(22.0%) had Apgar Score <7 at 5 minutes and required resuscitation. 4.0% neonates in TNG group and 14.0% neonates in placebo group developed respiratory distress syndrome, 6.0% neonates in TNG group required NICU admission and mechanical ventilator as compared to 12.0% neonates in placebo

group. 6.0% neonates were died in TNG group and 16.0% of neonates were died in the placebo group. Table (4)

## Discussion

Nitroglycerine is a drug with a high first pass inactivation in liver. The active substance is rapidly metabolized in the liver by a glutathione dependent organic nitrate reductase. To avoid it, transdermal use of the drug is beneficial. In transdermal drug administration the drug is delivered at a constant and predictable rate, so a smooth plasma concentration of the drug is reached without fluctuations. <sup>9</sup> This prospective randomized controlled trial was conducted in obstetrics and Gynecology department, AL- HUSSEIN University Hospital. The study was carried out on total of 100 patients with preterm labour. They were randomly assigned to either the nitroglycerine patch or bed rest alone. The duration of the study ranged from 6- 12 months.

As regard demographic data, in the TNG group the mean age of women was  $28.88 \pm 6.38$  greater than the mean age of women in the other group  $27.60 \pm 5.73$ . Preterm labor was more in multiparous women 41(82%) in TNG group and 38(76%) in the other group with no statistically significant difference between both groups ( $p$  value  $> 0.05$ ). The results demonstrated that 5(10.0%) of women had history of preterm labor and 23(46.0%) had a history of abortion as compared to 2(4.0%) and 20(40.0%) in the placebo group, respectively with no statistically significant difference between both groups ( $p$  value  $> 0.05$ ). Our results were supported by study of Bashir et al., <sup>2</sup> as they reported that in the first group nitroglycerine transdermal patch of 5 mg was applied over the anterior abdominal wall. Oral nifedipine was administered to all participants of second group. There was no significant difference between their studied groups as regard age and gestational age.

Similarly, AKHTAR et al., <sup>10</sup> revealed that patients of preterm labour were equally ( $n=63$ ) divided in two groups. In group A nitroglycerine was given to the patients whereas in group B, nifedipine was provided. Mean age of the patients in group A was  $29.96 \pm 4.32$  years with mean BMI  $25.70 \pm 4.12$  kg/m<sup>2</sup> and mean age among patients of group B was  $28.78 \pm 9.48$  years with mean BMI  $25.68 \pm 8.21$  kg/m<sup>2</sup>. The present study showed that there was no statistically significant difference between both groups as regard laboratory measures. Our results were in line with study of Shah et al., <sup>11</sup> as they reported that maternal outcome in terms of successful tocolysis & thereby prolonging the duration of period of gestation can be successfully achieved by using NTG patch in appropriate selected cases of preterm labour.

Our results were supported by study of Ghomian et al., <sup>4</sup> as they reported that the suppression of contractions 48 hours after starting medication was significantly more common in the GTN group than in the nifedipine group (44.64% ( $n = 25/56$ ) vs  $n = 10$ ,  $P = 0.002$ ). In addition, the delivery of women treated with GTN was more prolonged in comparison to those treated with nifedipine (34 - 6 vs 33 - 5,  $P = 0.012$ ). Another study carried out by Kashanian et al., <sup>12</sup> reported that in females treated with nitroglycerine (NG), delivery was postponed for 2 hours,

moreover, after 48 hours; the deliveries remained postponed in nitroglycerine (NG) group compared to nifedipine group, favouring our results.

Also, in the study of Jamil et al., <sup>9</sup>, the mean prolongation of pregnancy was  $14.98 \pm 2.01$  days in Group I (TNG) versus  $17.09 \pm 2.61$  days in Group II (nifedipine), which was not statistically significant. However, failure of acute tocolysis, defined as delivery within 48 hours, was significantly more with nifedipine (16/50 women-32%) as compared to NTG (6/50 women-12 %). The current study showed that the most common side effect noticed among the mothers was headache 8(16.0%) followed by hypotension 4(8.0%), vomiting 3(6.0%) and irritation 3(6.0%) at patch site.

In accordance with our results study of Jamil et al., <sup>9</sup> as they reported that among maternal side-effects, headache was significantly higher in the nifedipine group compared to nitroglycerine group (24/50, 42 % versus 2/50, 4%, p value 0.001). Hypotension was exclusively seen with nifedipine (2 women- 4.7%). However, the incidence of other maternal complications was not significantly different in the two groups. More number of women required discontinuation of treatment with nifedipine (4/50, 8%) compared to nitroglycerin (1/50, 2%). However statistical difference could not be established.

Similarly, in the study of Shah et al., <sup>11</sup> headaches occurred in 70% women of study Group (TNG). The severity of headache in was found to be mild in 70% of women and moderate in 30% of women which was relieved by Tab. Paracetamol 500 mg 1 tab stat. However, none of the women suffered from severe headache. Palpitation was observed in 4% of the women. The effect of TNG on pulse and blood pressure was not significant. The side effects were not so severe that required drug discontinuation

Our results showed that regarding the neonatal outcomes, the results of the study showed that all the (100%) babies were born alive. Birth weight of more than 2.4 kg was noted in 20 (40.0%), while 18 (36.0%) were born with birth weight between 2.2 to 2.4kg, 7 (14.0%) babies had weight of 1.9kg to 2.1kg and only 5 (10.0%) had weight of less than 1.8kg in the TNG group as compared to 8(16.0%), 17(34.0%), 17(34.0%) and 8(16.0%) respectively in the other group with statistically significant difference between both groups (p value<0.05).

In the study of Jamil et al., <sup>9</sup>, there was no significant difference in the neonatal outcomes and complications like respiratory distress syndrome (RDS), birth asphyxia, hypoglycemia, sepsis, need for neonatal intensive care unit (NICU) admission and mean duration of stay. Neonatal Jaundice was the commonest complication 48/100 women (48%) followed by RDS 12/100 (12%). In addition, Ghomian et al., <sup>4</sup> revealed that women treated with GTN, their babies had significantly higher Apgar scores of minutes one and minute five ( $7.6 \pm 0.88$  vs  $7.0 \pm 0.71$ ,  $P = 0.001$  and  $8.3 \pm 1.05$  vs  $7.6 \pm 1.12$ ,  $P = 0.001$ , respectively). Furthermore, Shah et al., <sup>11</sup> demonstrated that APGAR score was >7 in 92% in study group. 8% babies had APGAR < 7. All those babies who had APGAR < 7, required resuscitation. Only 8% neonates had APGAR Score < 7 and required resuscitation. 2% neonates developed respiratory distress syndrome. In study

group only one baby required mechanical ventilation due to development of severe RDS.

## Conclusion

TNG appear to be at least as effective as the commonly used tocolytics today. NTG patch may prove to be the drug of choice for acute uterine relaxation in cases of preterm labour. This randomized prospective comparative study lends support to the preposition that Transdermal Nitroglycerine may be promising, safe, effective, well tolerated, cost effective and noninvasive method of tocolysis.

**Conflict of interest:** no conflicts of interest.

## References

1. Haram K, Mortensen JH, Morrison JC. Tocolysis for acute preterm labor: does anything work. *The Journal of Maternal-Fetal & Neonatal Medicine*, 2015; 28(4), 371-378.
2. Bashir B, Shafiq M, Nazir A, Alam MA, Taimoor A. Effectiveness of transdermal nitroglycerine compared to oral nifedipine in prevention of preterm labour. *Pakistan Journal of Physiology*, 2019; 15(4), 7-10.
3. Pimenta JM, Ebeling M, Montague TH, Beach KJ, Abell J. A retrospective database analysis of neonatal morbidities to evaluate a composite endpoint for use in preterm labor clinical trials. *American Journal of Perinatology Reports*, 2018; 8(01), e25-e32.
4. Ghomian N, Vahedalaian SH, Tavassoli F, Pourhoseini SA, Heydari ST. Transdermal nitroglycerin versus oral nifedipine for suppression of preterm labor. *Shiraz E-Medical Journal*, 2015; 16(11-12).
5. Baker E, Hunter T, Okun N, Farine D. Current practices in the prediction and prevention of preterm birth in patients with higher-order multiple gestations. *American journal of obstetrics and gynecology*, 2015; 212(5), 671-e1.
6. Tavassoli F, Ghomian N, Hosseini S, Hosseini FS, Hosseini RS. Effectiveness of Nifedipine and Transdermal Nitroglycerin in Treatment of Preterm Labor. *Asian Research Journal of Gynaecology and Obstetrics*, 2020; 10-18.
7. Goyal N, Agrawal M. Comparative study of effectiveness of transdermal nitroglycerine patch and oral nifedipine in management of preterm labor. *European Journal of Molecular & Clinical Medicine*, 2020; 7(7), 2091-2098.
8. Kaur P, Madan A, Sharma S. A comparative study of transdermal nitroglycerine patch and oral nifedipine in preterm labor. *Annals of African Medicine*, 2021; 20(1), 31.
9. Jamil M, Abid R, Basharat A. Transdermal nitro-glycerine versus oral Nifedipine for Acute Tocolysis in Preterm Labour: A randomised controlled trial. *Journal of the Society of Obstetrics and Gynaecologists of Pakistan*, 2020; 10(1), 26-29.
10. Akhtar Z, Amna B, Qamar S, Saddiqua A, Bibi N, Bibi S. Compare the Effectiveness of Transdermal Nitro-Glycerine versus Oral Nifedipine for Acute Tocolysis in Preterm Labour. *P J M H S* 2020; 14(4).
11. Shah K, Gupta BD, Sharma R. "Dermal Nitroglycerin Patch" in Treatment of Preterm Labour. *Journal of Biosciences and Medicines*, 2015; 3(11), 82.

12. Kashanian M, Zamen Z, Sheikhsari N. Comparison between nitroglycerin dermal patch and nifedipine for treatment of preterm labor: a randomized clinical trial. *Journal of Perinatology*, 2014; 34(9), 683-687.