

## **Profile of Prematurity in Tobruk Medical Center Risk Factors, Complications, and Outcome 2017-2018**

*Nasren Gamal Saleh Al-Fraik<sup>1</sup>, Inas Ali Yhea<sup>2</sup>, Khadeejah Miftah Ali Al-Khurum<sup>1</sup> and Muftah Ahmad Otman<sup>1</sup>*

<sup>1</sup>Faculty of Medicine, Pediatric Department, Tobruk University, Tobruk ,  
Libya;

<sup>2</sup>Faculty of Medicine, Gynecology and Obstetrics Department, Tobruk  
University, Tobruk ,Libya.

**Corresponding author:** Nasren Gamal Saleh Al-Fraik, Assistance Lecturer,  
Tobruk Medical Collage, Eshbelia Street, Tobruk, libya

### **Abstract**

*: Preterm birth is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health. The main target in our study is to determine the risk factors, complications, outcome and incidence of prematurity in Tobruk Medical Center. This prospective study was conducted on 174 preterm neonates which delivered at Tobruk Neonatal Intensive Care Unit from January 2017 to January 2018. The 174 preterm newborns were aged between 28 to 36 weeks. The main risk factor is maternal (48%), fetal (24%) and idiopathic (20%). The maternal risk factors for preterm delivery were (27.5%) with premature rupture of membranes, (23.5%) urinary tract infection, (13.2%) with vaginal infection, (13.2%) idiopathic, (12.6%) have bleeding, (10.9%) hypertensive, (9.7%) diabetic and (1%) other causes. The complications present were respiratory (33.9%), sepsis (22.9%), apnea (17.8%), metabolic (8.6%), central nervous system (6.8%), congenital malformation (6.8%), and gastro intestinal complication was (0.5%). Outcome was 126 discharged (72.4%), 44 died (25.2%), and 4 transferred (2.2%), cause of death was 85% respiratory, 14% sepsis, and 1% GIT (necrotizing enterocolitis). This study found that the incidence of prematurity was 22.8% in Tobruk Medical Center during one year. The predominant risk factor for prematurity was maternal and the respiratory was the most common complication.*

**Key Words:** Prematurity; Maternal factors; Complications; Outcome..

## INTRODUCTION

Preterm birth defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation. It is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health <sup>[1,2]</sup>. The birth of premature infants is associated with several problems, such as frequent hospital admissions, infections, apnea and others <sup>[3]</sup>. Despite the comprehensive efforts to prevent premature delivery and birth of premature infants, the birth rates of such infants are high due to some medical problems, social status and infertility treatment <sup>[4,5]</sup>. In the United States, there are about 250,000 premature and low birth weight infants each year, accounting for 8.8% of births <sup>[6]</sup>. In 2010, approximately 15 million babies were born preterm, and more than 1 million died due to complications during the first month of life<sup>[9]</sup>. In Iran, 5000 neonates are born daily, about 12% of them are underweight.<sup>[7]</sup> Globally, among all neonatal deaths in 2013, 35% cases were caused by preterm birth complications alone.<sup>[8]</sup> Research that expands our understanding of the causes and risk factors of preterm birth and how to identify women and adolescents at risk is particularly needed to decrease the global neonatal mortality rate.<sup>[9]</sup> Without accurate, comprehensive background information describing the existing state of preterm neonatal births, risk factors, and national mortality, an international improvement in preterm neonatal care would be extremely challenging to achieve. Despite a progressive decline in neonatal mortality rates between 1990 and 2013, the national neonatal mortality rate remains high, at 11 neonatal deaths per 1000 live births in 2013.<sup>[8]</sup> Population-based studies reporting the outcomes of preterm birth using standardized mortality definitions are highly recommended in low- and middle resource settings.<sup>[10]</sup> Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term. The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs.<sup>[11,12]</sup> In recent years, the care provided in Neonate Intensive Care Units (NICU) settings increased the survival of premature infants but at the same time increased duration of hospitalization and costs. As a result, the care of premature neonates currently accounts for a large proportion of the total in-hospital costs worldwide.<sup>[13]</sup> the frequency of preterm labor varies considerably between countries, almost 90% of these premature births occur in developing countries in Africa and Asia.<sup>[14]</sup> In 2014, the rate of preterm births was 10% in the US <sup>[15]</sup> while in Europe in 2010, preterm birth rates varied markedly from 5 to 10.6% among live births.<sup>[16]</sup> Cyprus is characterized by the highest premature birth rate in Europe, reaching 10.6% and 13.1% in 2010 and 2014 respectively.<sup>[17, 18]</sup> partly due to increase of multiple pregnancies following in-vitro fertilization.<sup>[19]</sup> Ethiopia is among the top 15 countries that contribute to two-thirds of the world's preterm babies with an estimated preterm birth rate of 14.1%.<sup>[20]</sup> In 2015, 5.9 million children under

the age of five died across the globe. Of these, 44% or 2.6 million deaths occurred within the first month of life. Just over a third of these babies died as a result of prematurity-related causes.<sup>[21]</sup> Estimates indicate that in 2005, the costs to the United States of America alone in terms of medical and educational expenditure and lost productivity associated with preterm birth were more than US\$ 26.2 billion.<sup>[22]</sup> Of all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.<sup>[23]</sup> Complications from preterm births are the leading direct cause of neonatal deaths accounting for 35% of all newborn deaths, and are also a contributing cause in an additional 40 to 60% of neonatal deaths. Mortality rates increase proportionally with decreasing gestational age or birth weight <sup>[24, 25]</sup>. In Ethiopia, of the estimated 91,700 neonatal deaths in 2010, more than one-third were estimated to be due to complications of preterm birth <sup>[26]</sup>. Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries.<sup>[27]</sup> Approximately 45–50% of preterm births are idiopathic, 30% are related to preterm rupture of membranes (PROM) and another 15–20% are attributed to medically indicated or elective preterm deliveries.<sup>[28,29]</sup> Estimation of preterm birth rates and their proper categorization (e.g. spontaneous versus indicated) are essential for accurate determination of global incidence in order to inform policy and programs on interventions to reduce the risk of premature labor and delivery.<sup>[30]</sup> No data have been published on the global incidence of preterm birth. Preterm birth rates available from some developed countries, such as the United Kingdom, the United States and the Scandinavian countries, show a dramatic rise over the past 20 years.<sup>[30]</sup> Changes in the definitions of fetal loss, stillbirth and early neonatal death may also have contributed to the substantial increases in preterm birth rates recorded in developed countries in the past two decades.<sup>[31]</sup>

In addition to determining the causes of preterm birth, a better understanding of the events leading to deaths in preterm infants is needed. Similar to term infants, preterm infants may suffer from multiple morbidities, such as sepsis, asphyxia, respiratory distress syndrome, major congenital malformations, and metabolic disorders <sup>[32, 33]</sup>. In developing countries, accurate and complete population data and medical records usually do not exist. Furthermore, estimates of the rate of preterm birth in developing countries are influenced by a range of factors including varying procedures used to determine gestational age, national differences in birth registration processes, heterogeneous definitions used for preterm birth, differences in perceptions of the viability of preterm infants and variations in religious practices such as local burial customs, which can discourage the registering of preterm births<sup>[34]</sup>. Preterm birth (PTB, <37 gestational weeks) has become an increasingly important global health concern, because of its association with infant mortality.<sup>[35]</sup>

## Materials and Methods

This Prospective study over 12 months period was conducted on 174 premature babies admitted in the nursery of Tobruk Medical Center from January 1<sup>st</sup> 2017 to January 1<sup>st</sup> 2018.

**Inclusion criteria:** This study includes all preterm newborns admitted in the nursery.

No exclusion criteria.

**Interventions:** All mothers were subjected to complete history file including age of gestation from the last menstrual period or ultrasound in the first trimester, history of urinary tract infection, vaginal infection, symptoms of chorioaminionitis, as foul smelling vaginal discharge, fever and abdominal Pain, time of onset and duration of premature rupture of membranes & administration of antenatal corticosteroids. All newborns were subjected to complete history file thorough clinical examination including vital signs (Heart rate, respiratory rate and blood pressure) anthropometric measurements (birth weight, length and skull circumference), mode of delivery and APGAR score. Detailed clinical examination of all body systems, feeding history include types and onset of feeding. **Laboratory:** All newborns were subjected to: random blood sugar, serum electrolytes as Na, K, Ca, renal & liver function when needed. Complete blood picture: a sample collected through venipuncture from all preterm neonates. **Radiology:** Chest X-ray for preterm newborns with respiratory distress. Other investigations as cranial and abdominal ultrasonography were done as needed. **Statistical analysis (Using standard computer program):** The description of data was in the form of mean ( $\pm$ )SD for quantitative data, and frequency and proportion for qualitative data.

## Results and Discussion

This study performed on 174 preterm newborns, (52,2% males and 47,7% females), with gestational age arranged from (28-36 weeks) and birth weight varied from (670-2900 grams). Duration of admission arranged from (1-40 days).

**Table:(1)**Demographic Data of Premature Babies

Demographic data	Cases (174)	
	No.	%
	Mean $\pm$ SD	
Gestational age in weeks	32.10	
Birth weight by grams	1876.173	

## Profile of Prematurity in Tobruk Medical Center Risk Factors, Complications, and Outcome 2017-2018

Gender	Male	91	52.2%
	Female	83	47.7%

**Table (2)** Risk Factors for Preterm Delivery

Risk Factor	Percentage %
Maternal	48%
Fetal	24%
Placental	%1
Idiopathic	20%

Maternal Risk Factors for Prematurity **Table (3)**

Maternal risk factor	Number	Percentage%
PROM	48	27.5%
UTI	41	23.5%
Vaginal infection	23	13.2%
Idiopathic	23	13.2%
Bleeding	22	12.6%
HTN	19	10.9%
DM	17	9.7%
Other causes	2	1.1%
HELLP	1	0.5%
Preceipitatedlabour	1	0.5%

Complications among Studied Premature Newborns **Table (4)**

Complication	Number	Percentage%
RDS	59	33.9%
Sepsis	40	22.9%
Apnea	31	17.8%
Metabolic	15	8.6%
Congenital malformation	12	6.8%
CNS	12	6.8%
GIT	1	0.5%

Premature Studied Outcome of **Table(5)**

Outcome	Number	Percentage%
Discharged	126	72.4%
Died	44	25.2%
Transferred	4	2.2%

**Table Abbreviations:**UTI:Urinary Tract Infection, DM: Diabetes Mellitus, HTN: Hypertension, HELLP: Hemorrhage Elevated Liver enzyme Lower Platelet, PROM: Premature Rupture Of Membrane, RDS: Respiratory Distress Syndrome, CNS: Central Nervous System, GIT: Gastrointestinal Tract.

The complications were respiratory(51.7%), metabolic(8.6%),gastrointestinal(0.5%), sepsis (22.9%) and central nervous system(6.8%). This disagree with a previous study reported thatIVH, BPD, ROP,NEC , pneumothorax and DIC were common complications in the neonatal unit that could responsible for a large number of morbidity and mortality.<sup>[36]</sup>

This study found the incidence of prematurity 22.8% in Tobruk Medical Center 2017, while the incidence in US was 12,8% in 2006 and decline to 11.73% in 2011. Italy saw a modest increase from 5,8% in 1990 to 6.5% in 2010, consistent with other European countries.

While a previous studyestimated that in 2005, 12.9 million births, or 9.6% of all births worldwide, were preterm. Approximately 11 million (85%) of these preterm births were concentrated in Africa and Asia, while about 0.5 million occurred in each of Europe and North America (excluding Mexico) and 0.9 million in Latin America and the Caribbean.<sup>[37]</sup> The highest rates of preterm birth were in Africa and North America (11.9% and 10.6% of all births, respectively), and the lowest were in Europe (6.2%).Preterm babies contribute 31.06% of the total admissions, 10.18% of the total admissions were preterm babies.<sup>[38]</sup>

In general, gestational diabetes mellitus has been found to be associated with medically indicated premature labor and lower gestational age.<sup>[39, 40]</sup> However, in our study, we found that the frequency of gestational diabetes was lower in mothers who had premature birth compared to controls. Similar negative associations between pregnancy outcomes and gestational diabetes have been also reported by few recent studies <sup>[41, 42]</sup>. These discrepancies can be attributed to the possibility of good glycemic control of women with gestational diabetes in these studies through good obstetric monitoring, balanced diet and insulin treatment, factors which have not been specifically assessed in our study <sup>[43, 44]</sup>. A recent study demonstrated that although presence of uncontrolled gestational diabetes and obesity during pregnancy is associated with negative prognosis, their effects can be counterbalanced by the application of glycaemic control combined with controlled weight gain <sup>[45]</sup>. Furthermore, comparison with previous studies is inherently difficult as the effect of gestational diabetes on perinatal outcomes is influenced by racial factors <sup>[46]</sup>, the different diagnostic criteria for gestational diabetes that are used in each country, the heterogeneity of study populations and differences in the detection programs that are applied in each country, which eventually result in a wide range of gestational diabetes frequency from less than 1% to above 10% across the world.<sup>[43]</sup> UTI in pregnancy was associated with premature birth. This was similar to the findings of studies in Iran and Nigeria.<sup>[48, 47]</sup> Results of the current study demonstrated that after controlling for confounders, prolonged PROM, PIH and APH



remained significantly associated with preterm birth. These findings are similar to those reported in other studies. PROM has been associated with chorioamnionitis which may be subclinical and chlamydial vaginitis. Microorganisms that cause bacterial vaginosis can easily ascend in prolonged PROM and cause intrauterine infections. It is postulated that subclinical chorioamnionitis and other unidentified infections may trigger the release of inflammatory mediators such as interleukin 1 leading to release of prostaglandins from the uterine decidua that ultimately induce preterm labor. PIH which is one of the major obstetric complications was significantly associated with PTB in the current study. Though the pathophysiology of this condition remains poorly understood, uteroplacental ischemia is a plausible explanation for the poor pregnancy outcomes associated with PIH including preterm delivery and low birthweight. Furthermore, PIH is a common reason for indicated preterm deliveries and this may explain its association with PTB even though this may not be causal in nature. Like PIH, APH is also a major contributor to indicated preterm deliveries whether vaginally or operatively without necessarily having a temporal relationship with PTB <sup>[49, 48, 47]</sup> This study identifies mothers with prolonged PROM, PIH and APH as a high risk group for PTB. These are largely modifiable factors and should form a good basis for prenatal interventions and better management geared towards reducing the burden of PTB. The best intervention for prevention of spontaneous preterm birth in women with risk factors is still unclear.<sup>[50]</sup> However, simple cost-effective and research-supported interventions are available to reduce deaths among premature babies;

For example, the promotion of early and exclusive breastfeeding, handwashing, and innovative skin-to-skin care.<sup>[51, 52]</sup> The prevention of hypothermia and management of respiratory distress syndrome, neonatal pneumonia, sepsis, and hyperbilirubinemia are evidence-based interventions that can greatly increase the survival of small and sick neonates<sup>[51]</sup>. Globally, 4 out of 5 newborn deaths result from three preventable and treatable conditions, primarily prematurity.<sup>[52, 53]</sup> Prematurity is often complicated by infections and respiratory complications, which commonly leads to the death of preterm infants.<sup>[54]</sup> These complications can be prevented and treated by skilful and high-quality postnatal care of preterm neonates, especially during the first week of life. The identification of warning signs during pregnancy is an important goal of antenatal care.<sup>[55]</sup> Preeclampsia, diabetes, and hypertension, whether pre-existing or gestational, are maternal medical conditions that commonly predict preterm birth<sup>[56]</sup>, (a finding that is similar to those of this study.

## **Conclusion**

Addressing the major risks associated with the incidence and the mortality of preterm neonates is a priority to reduce the global burden of preterm birth, along

with identifying areas that are crucial to improve the health care systems across countries. The main result of this study found the incidence of prematurity is still high in Tobruk Medical Center. The main risk factor for prematurity was maternal and the main maternal risk factor was PROM and UTI. The main complication was respiratory followed by sepsis. 25% of admitted preterm babies were died. Prevention of prematurity by prevention and control of maternal risk factors is very important target and needs more effort and planes. Plane for prevention and treatment of complication of premature babies to improve outcome is the main target in our center.

### **Acknowledgements**

The authors thank all neonatal intensive care unit staff, mothers of premature newborn and their babies.

### **References**

- 1-International classification of diseases and related health problems.(1992). 10th revision. Geneva: *World Health Organization*.
- 2-Wang M.L., Dorer D.J., Fleming M.P., Catlin E.A.et.al.(2004).Clinical outcomes of near-term infants. *Pediatrics*;114:372-6. *PMID*:15286219 doi:10.1542/peds.114.2.372
3. Ahmadi SH, Kazemi F, Masoumi SZ, Parsa P, Roshanaei G.(2016) Intervention based on BASNEF model increases exclusive breastfeeding in preterm infants in Iran: a randomized controlled trial. *International Breastfeeding Journal*;11:30.
4. Masumi Z, Parsa P.( 2015) An epidemiologic survey on the causes of infertility in patients referred to infertility center in Fatemieh Hospital in Hamadan. *Iranian Journal of Reproductive Medicine*;13(8):513–516.
5. Mirlashari J, Rassouli M. AndishehRafee. 1st ed. Tehran.(2007). Nursing care of infant and children; pp. 70–1.
6. Aagaard HR, Hall RN.(2008). Mothers' next term experiences of having a preterm infant in the Neonatal previous term Care next term Unit: a Meta-Synthesis. *Journal of Nursing Pediatric*; 23(3):e26–36.
7. Sarparast L, Farhadi R, Sarparast M, Shafai S.(2015). The Effect of Kangaroo Mother Care on Neonatal Outcomes in Iranian Hospitals: a review. *J Pediatric Review*.;3(1):e195.
- 8.UN-IGME TI-AGfCME. (2014). Levels & Trends in Child Mortality Report.United Nations Children's Fund.
9. HowsonCP, KinneyMV, LawnJE. (2012). Born Too Soon: The Global Action Report on Preterm Birth. WHO, Geneva.
10. Gladstone M, Oliver C. (2015). Survival, morbidity, growth and developmental delay for babies born preterm in low and middle income countries - a systematic review of outcomes measured. *PLoSOne*;10:e0120566.



11. Petrou S., Mehta Z., Hockley C., Cook-Mozaffari P., Henderson J., et.al.(2003).During the first 5 years of life. *Pediatrics*;112:1290-7. doi:10.1542/peds.112.6.1290
- 12-Petrou S.(2005).The economic consequences of preterm birth during the first 10 years of life.*BJOG*;112Suppl 1;10-5.
13. Comert S, Agzikuru T, Akin Y, Telatar B, Tan PD, et.al. (2012). The cost analysis of preterm infants from a NICU of a state Hospital in Istanbul. *Iran J Pediatr.*;22(2):185–190.
14. Beck S, Wojdyla D, Say L, Pilar BA, Meraldi M, et.al.(2010). The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bulletin of the World Health Organization* ;88(1):31–38. doi: 10.2471/BLT.08.062554.
15. Center for Disease Control and Prevention, Preterm Birth.(2018). Available from:[<https://www.cdc.gov/reproductivehealth/maternalinfanthealth/preterm-birth.htm>].
16. Delnord M, Blondel B, Zeitlin J.(2015). What contributes to disparities in the preterm birth rate in European countries?. *CurrOpinObstetGynecol.* ;27(2):133–142. doi: 10.1097/GCO.0000000000000156.
17. Macfarlane A, Dattani N. (2010) European Perinatal Health Report Health and care of pregnant women and babies in Europe in 2010.
18. Cyprus Health MonitoringUnit. (2014). Perinatal health indicators for the year 2014, [<https://www.moh.gov.cy/Moh/MOH.nsf/All/8DC461429CBC4DE7C22579CE002EF07D?OpenDocument>].
19. Zeitlin J, Szamotulska K, Drewniak N, MohangooA, Chalmers J, et.al.(2013). Preterm birth time trends in Europe: a study of 19 countries. *BJOG Int J ObstetGynaecol.* 2013;120(11):1356–1365. doi: 10.1111/1471-0528.12281.
20. Adane AA, Ayele TA, Ararsa LG, Bitew BD, Zeleke BM.(2014)Adverse birth outcomes among deliveries at Gondar University hospital, Northwest Ethiopia. *BMC Pregnancy Childbirth*;14:90. doi: 10.1186/1471-2393-14-90.
21. Liu L, Johnson HL, Cousens S, Perin J, Scott S, et al.(2015). Global, regional, and national causes of child mortality in 2000–13. *Lancet*;385:430–444. doi: 10.1016/S0140-6736(14)61698-6.
- 22- PeriStats [online database].(2006). White Plains, NY: March of Dimes. Available from: <http://www.marchofdimes.com/peristats/>
- 23-Lawn J.E., Wilczynska-Ketende K., Cousens S.N.(2006). Estimating the causes of 4 million neonatal deaths in the year .*Int J Epidemiol*;35:706-18. PMID:16556647 doi:10.1093/ije/dyl043.
24. Beck S, Wojdyla D, Say L, Betran A, Merialdi M, et al. (2010).The worldwide incidence of preterm birth: a systematic review of maternal

- mortality and morbidity. *Bull World Health Organ*;88:31–38. doi: 10.2471/BLT.08.062554.
25. Allen MC, Alexander GR, Tompkins ME, Hulsey TC. (2000). Racial differences in temporal changes in newborn viability and survival by gestational age. *PaedPeriEpid.*;14:152–158.
  26. Shah PS, Lui K, Sjörs G, Mirea L, Reichman B, et al. (2016). International network for evaluating outcomes (iNeo) of neonates. Neonatal outcomes of very low birth weight and very preterm neonates: an international comparison. *J Pediatr.* 2016;177:144–152. doi: 10.1016/j.jpeds.2016.04.083.
  27. Lawn J.E., Cousens S.N., Darmstadt G.L., Bhutta Z.A., Martines J., et al. (2006). 1 year after The Lancet Neonatal Survival Series — was the call for action heard? *Lancet*;367:1541-7. doi:10.1016/S0140-6736(06)68587-5
  28. Haas DM. (2006). Preterm birth in clinical evidence. London: BMJ Publishing Group 28.
  - 29-Pennell C.E., Jacobsson B., Williams S.M., Buus R.M., Muglia L.J., et al. (2007). Genetic epidemiologic studies of preterm birth: guidelines for research. *Am J Obstet Gynecol*;196:107-18. doi:10.1016/j.
  - 30-Callaghan W.M., MacD.M.F., Rasmussen S.A., Qin C., Lackritz E.M. (2006). The contribution of preterm birth to infant mortality rates in the United States. *Pediatrics*;118:1566-73. doi:10.1542/peds.2006-0860.
  - 31-Davidoff M.J., Dias T., Damus K., Russell R., Bettgowda V.R., et al. (2006). Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. *Semin Perinatol*;30:8-15. doi:10.1053/j.semperi.2006.01.009
  32. World Health Organization. Maternal, Newborn and Child and Adolescent health. (2016). [http://www.who.int/maternal\\_child\\_adolescent/epidemiology/en/](http://www.who.int/maternal_child_adolescent/epidemiology/en/) Accessed 08 Jan 2017.
  33. Bang A, Reddy HM, Bang RA, Deshmukh MD. (2005). Why do neonates die in rural Gadchiroli, India? (part II): estimating population attributable risks and contribution of multiple morbidities for identifying a strategy to prevent deaths. *J Perinatol.*;25:S35–S43. doi: 10.1038/sj.jp.7211270.
  - 34-Graafmans W.C., Richardus J.H., Macfarlane A., Rebagliato M., Blondel B., et al. (2001). Comparability of published perinatal mortality rates in Western Europe: the quantitative impact of differences in gestational age and birth weight criteria. *BJOG*;108:1237-45.
  - 35-Black R.E. , Cousens S., Johnson H.L., Lawn J.E., Rudan I., et al. (2008). Global, regional, and national causes of child mortality : a systematic analysis. *Lancet.*;375:1969–87.
  - 36-Teresa C. , Marian K. , Ctirad A. , Marcela D. , Ivana M. , ( .2013). Umbilical cord blood IL-6 as predictor of early-onset neonatal sepsis in women with preterm prelabour rupture of membranes. *PLoS One* ; 8(7): e69341. doi: 10.1371 / journal. pone.0069341

- 37-World Health Organization.(2010). *WHO*;88:31–38 |doi:10.2471/BLT.08.062554.
- 38-Nandini K, Balasubramanian M, and Krithiga M..(2016). Issue 1 Magnitude of Preterm Admissions in Neonatal Intensive Care Unit of Rural Medical College Hospital. *International Journal of Scientific Study*; Vol 4.
39. Gasim T.(2012). Gestational diabetes mellitus: maternal and perinatal outcomes in 220 saudi women. *Oman Med J*.;27(2):140–144. doi: 10.5001/omj.2012.29.
40. Köck K, Köck F, Klein K, Bancher-Todesca D, Helmer H. (2010).Diabetes mellitus and the risk of preterm birth with regard to the risk of spontaneous preterm birth. *J Matern Fetal Neonatal Med*.;23(9):1004–1008. doi: 10.3109/14767050903551392
41. Mahalakshmi MM, Bhavadharini B, Maheswari K, Anjana RM, JebaraniS,et.al, (2016). Current practices in the diagnosis and management of gestational diabetes mellitus in India (WINGS-5). *Indian J EndocrinolMetab*. ;20(3):364–368. doi: 10.4103/2230-8210.180001.
42. Aviram A, Guy L, Ashwal E, Hirsch L, Yogev Y, et.al.(2016). Pregnancy outcome in pregnancies complicated with gestational diabetes mellitus and late preterm birth. *Diabetes Res Clin Pract*.;113:198–203. doi: 10.1016/j.diabres.2015.12.018.
43. Xiong X, Saunders L, Wang F, Demianczuk N.(2001). Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *Int J Gynecol Obstet*.;75(3):221–228. doi: 10.1016/S0020-7292(01)00496-9.
44. Au CPY, Raynes-Greenow CH, Turner RM, Carberry AE, Jeffery HE.(2016). Antenatal management of gestational diabetes mellitus can improve neonatal outcomes. *Midwifery*;34:66–71. doi: 10.1016/j.midw.2016.01.001.
45. Benhalima K, Robyns K, Van Crombrugge P, Deprez N, Seynhave B, et.al.(2015). Differences in pregnancy outcomes and characteristics between insulin-and diet-treated women with gestational diabetes. *BMC pregnancy and childbirth*; 15(1):271.
46. Silva JK, Kaholokula JK, Ratner R, Mau M. (2006).Ethnic differences in perinatal outcome of gestational diabetes mellitus. *Diabetes Care*;29(9):2058–2063. doi: 10.2337/dc06-0458.
47. Muglia LJ, Katz M.(2010).The enigma of spontaneous preterm birth. *N Engl J Med*. 2010;362:529–535. doi: 10.1056/NEJMra0904308.
48. Goyal SC, Tak SK, Bhandari B. (1989).Determination of gestational age: comparative accuracy of different methods. *Indian J Pediatr*. ;56(1):115–119. doi: 10.1007/BF02749722.
49. Goldenberg RL, Culhane JF, Iams JD, Romero R. (2008).Epidemiology and causes of preterm birth. *Lancet*. ;371:75–84. doi: 10.1016/S0140-6736(08)60074-4.

50. Stock SJ, Ismail KM.(2016). Which intervention reduces the risk of preterm birth in women with risk factors? *.BMJ*;355:i5206.
51. Bhutta ZA, Das JK, Bahl R, Lawn JE, Salam RA, et al.(2014). Can available interventions end preventable deaths in mothers, newborn babies, and stillbirths, and at what cost?. *Lancet*;384:347–70.
52. Lawn JE, Davidge R, Paul VK, von Xylander S, Costello A, et al. (2013).Born too soon: care for the preterm baby. *Report Health*;10Suppl 1:S5.
53. Save the Children Federation. (2012). Improving Newborn Survival: Saving the Lives of 3 Million Save the Children Federation, Inc.
54. Patel RM, Kandefer S, Walsh MC, Bell EF, Carlo WA, et al. (2015).Causes and timing of death in extremely premature infants from 2000 through 2011. *N Engl J Med.* ;372:331–40.
55. World Health Organization. (2015). Global Health Observatory Data (GHO).
56. Donoghue D, Lincoln D, Morgan G, Beard J. (2013).Influences on the degree of preterm birth in New South Wales. *Aust N Z J Public Health*;37:562–7.
- 57-Stacy B,Daniel A, Wojdyla B, Say, CA, Pilar B, Mario M,Jennifer H, Requejo,dCR,Ramkumar M, Paul FVL . The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity.