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Stress Indicators For Newborn Infants Undergoing Phlebotomy

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Abstract: Newborn infants experience stress associated with commonly used invasive procedures such as venipuncture. Therefore, reduction of neonatal stress is very important because untreated stress has adverse effects. This study aimed at evaluating stress indicators for neonate infants undergoing phlebotomy procedures. Descriptive design was used. The study was conducted at all neonatal intensive care units of general hospitals in Port-Said Governorate, Egypt. A convenient sample of 130 newborn infants was included in this study. Data was collected by stress assessment scale to assess indicators of neonatal stress before, during and after venipuncture procedures. Results revealed that, the majority of newborn infants suffered from stress during phlebotomy procedures as assessed by physiological, autonomic, motor and behavioral indicators, while neonate infants did not have any change in these indicators before and after phlebotomy, except behavioral indicators. Motor indicators of the neonate infants showed the highest percentage of neonatal stress during phlebotomy procedures. Statistically significant differences were found. The study concluded that, there were statistically significant differences between physiological, autonomic, motor and behavioral indicators and total stress for neonate infants undergoing phlebotomy procedures. An educational training program on non-pharmacological methods for pediatric nurses in neonatal intensive care units is recommended to reduce stress for neonate undergoing phlebotomy procedures.

Key words: Newborn • Neonate • Full-Term • Pre-Term • Stress • Painful Procedure • Venipuncture • Pediatric Nursing • Physiological Indicators • Motor Indicators • Behavioral Indicators

• Autonomic Indicators • Stress Indicators • Phlebotomy

INTRODUCTION

The word of newborn means an infant who is less than four weeks old. It comes from the word "Neonate"; "Neo" means new and "nat" means born. This period is considered the most vulnerable period of life, during which many psychological and physiological changes occur to adjust neonate to the extra-uterine life. The majority of infant deaths occur in this period. So, the care provided by pediatric nurses in the Neonatal Intensive Care Units (NICUs) during the first month of life is pivotal and affect this adjustment [1].

Stress is defined as "A physical, chemical, or emotional factors that cause bodily or mental tension" It compounds a variety of neonatal infant's reactions when faced stressors [2, 3].

Neonates exposed to many stressors in the hospital environment. Bright light, noisy sounds of equipment and pediatric nursing care disturb rest and bring discomfort for the newborn infants. These are the principal stressors in the NICU. These environmental stressors are damaging to newborn infants who is hospitalized [4, 5]. It has both immediate and long-term harmful effects on the neonatal health. It can alter their physical and physiological growth and their development. Also, affect the development of neonatal central nervous system. 30 to 60% of high risk neonate infants will suffer from cognitive, social and emotional difficulties during their lives. Recent research has shown that NICU stress is correlated with brain injury and impaired brain development [6, 7].

The neonates daily exposure to approximately 16 stressful procedures as nasal and endotracheal suction and adhesive tape removal, during intensive care period in the first 14 days of their lives. Moreover, these pediatric nursing interventions may be administered with no attention to stress reduction measures and this in turn has negative consequences on the health of newborn infants. As well as, non-painful procedures as changing position or administration of medicine and diaper change also can cause stress responses in high risk neonates [8].

Phlebotomy which comes from the Greek words "Phleba-", meaning "Vein" and "-tomy," meaning "To make an incision of" is the process of taking blood from a vein with a needle. The procedure is known as a venipuncture [9]. Venipuncture which comprises 8-13% of invasive procedures is an essential and frequently performed procedure in neonate admitted to NICU. It is considered as one of the most difficult practices producing moderate to severe pain in neonates. Yearly, millions of newborns need blood tests for diagnosis cry and exhibit facial expression and body movements due to pain and distress [10-12].

Pain is "A stressor that stimulates the sympathetic nervous system to produce the fight or flight response leading to physiological and behavioral changes including increase in heart rate, peripheral vasoconstriction, diaphoresis, pupil dilation increased secretions of catecholamine, adrenocortical, thyroid and pancreatic hormones. As well as, increase respiratory rate, decrease blood pressure and high oxygen saturation levels". In addition to, neonatal distress includes behavioral responses such as crying, grimace and body movements [13].

The impact of unrelieved pain and distress in newborn infants includes immediate effects as "irritability, fear, disturbance of sleep and wakefulness state, increased oxygen consumption, diminished nutrient intake, increased gastric acidity". Short term effects as "enhanced catabolism, altered immunological function, delayed healing" and "impaired emotional bonding", while long term effects include: "memory of pain, developmental retardation and alteration in response to subsequent painful experience" [14].

Pediatric nurses play a critical role in relation to stress indicators, they observe, assess and interpret stress indicators both behavioral and physiological throughout painful procedures and they respond to newborn infants to reduce their stress and thus in turn decrease consequent problems affect neonatal morbidity and mortality [15].

As a result of frequent painful procedures, which occur often without pharmacological and non-pharmacological pain management of neonates admitted to NICU, adverse outcomes will arise [16-18]. Furthermore, Neonate infant cannot self-report stress, which result in pediatric nurses not being able to recognize newborn's stress. As a result, behavioral and physiological indicators are needed to be assessed correctly and used to determine the treatment options for neonates So, for the importance of studying stress

indicators for newborn infants undergoing phlebotomy, this study was designed to meet their needs of caring for providing high quality nursing care for those infants.

Aim of the Study: The aim of the current study is to evaluate stress indicators for neonate infants undergoing phlebotomy procedures.

MATERIALS AND METHOD

Research Design: Descriptive design was used in the current study.

Study Setting: The present study was conducted at all neonatal intensive care units (NICU) in Port Said general hospitals namely; El-Nasr, Port-Said and Port-Fouad hospitals.

Subjects: A sample of the present study consisted of 130 newborns; 86 neonates from El-Nasr general hospital, 28 neonates from Port Fouad general hospital and 16 neonates from Port Said general hospital, from both sexes, aged from 1 day to 14 days; with different diagnoses include respiratory distress syndrome, jaundice, sepsis and prematurity. Their gestational age ranged from 35 weeks to more than 40 weeks, while their weight began with 1500 grams to more than 4000 grams. The sample was selected on the basis of convenience sampling technique from the previous mentioned settings. Newborns less than 1500 grams, or had congenital anomalies, neurological problems and taken analgesics or sedative treatment were excluded from the present study.

Tools of Data Collection: The stress assessment scale was used in the current study to assess indicators of neonatal stress before, during and after venipuncture procedures. It was developed by Modrcin-McCarthy *et al.* [19] and modified by Abd El-motalib [20] and Hassan [21]. The scale is divided into two parts:

Part I: Autonomic and physiological indicators of neonatal stress: It includes five items, namely, "heart rate, respiratory rate, blood pressure, oxygen saturation and skin color".

Part II: Motor and Behavioral indicators of neonatal stress: It includes five items, namely, "activity, overall tone, cry, facial expression and sleep pattern". The validity and reliability of the tool were 80 and 0.72% respectively.

Neonatal demographic data were obtained regarding gestational age, birth date, gender, weight, diagnosis and hospital admission date.

Scoring System of Neonatal Stress Tool: The response of the neonate infant to stress assessed before, during and after venipuncture procedures, ranges from 0-3 for each item in the scale.

The total percent scores of neonatal stress range from "0" to "30". It was calculated as follows:

The 0 score is considered no neonatal stress, 1-10 scores are considered mild neonatal stress 11-20 is considered a moderate neonatal stress. 21-30 is considered severe neonatal stress.

The scores of the items were summed up and the total (30) divided by the number of the items (10) giving a mean score for the part. These scores were converted into a percent score and means and standard deviations were computed.

Field Work: Data was collected from the previous mentioned settings. Before conduction of the study, an official letter was taken from the dean of the Faculty of Nursing in Port Said University to the directors of Port Said general hospitals, to obtain their approval. After an explanation of the purpose of the study, a written permission was secured from them. Neonatal demographic data were obtained from nursing and medical records. Data collection lasted for ten months, from 14/5/2015 till 12/3/2016. The researcher went to neonatal intensive care units, two followed days weekly in the morning shift from 9 am to 12 pm on the same group of neonates. The researcher filled some items in stress tool from ECG monitor as respiratory rate, heart rate, oxygen saturation and blood pressure. Other items were filled by observation as skin color, motor and behavioral responses.

Ethical Considerations: A verbal agreement was taken from every neonate's parent after a clear and simple explanation of the purpose of the study and that the information will be used for scientific research only and will be treated as confidential. A brief explanation of the study was given assured to the head nurses of the NICU and staff nurses who perform venipuncture procedures to gain their cooperation.

Statistical Analysis: Data collected were organized, coded, tabulated, computerized and analyzed by using

SPSS statistical program version 16. Descriptive statistics were used in the form of frequencies and percentages for qualitative data and means and standard deviations for quantitative data. Quantitative continuous data were compared using the Student t-test in case of comparisons between two groups. Qualitative categorical variables were compared using a chi-square test. Statistical significance was considered at P-value <0.05and p<0.001.

RESULTS

Regarding demographic characteristics, the present study consisted of 130 newborns, 62.3% were males and 37.7% were females, 92.3% had gestational ages ranging from 38 to 40 weeks and 80.8% born by caesarean section, 68.5% had weight 2500 grams to less than 3500 grams. 58.5% of newborns suffering from respiratory diseases, 46.2% took IV fluids and 55.4% of their hospitalization period were 10 to 14 days, with Mean score 4.70 ± 3.16 . 66.2% and 54.6% respectively of newborn infants had no stress before and after phlebotomy procedures, while 87.7% of them suffered from mild stress during these procedures. A statistical significant difference was found $(X^2=150.21, P=0.000)$ as seen in Table (1).

The results showed that more than two thirds of the sample (63.1% and 63.8%, respectively) had no autonomic and physiological stress before and after phlebotomy procedures compared to 70% of the sample had a mild degree of autonomic and physiological stress during these procedures with a statistical significant difference (X^2 =180.86, P=0.000) (Table 2).

The majority of newborn infants (98.5% and 99.2%, respectively) did not have any motor indicators of stress as a change in neonatal activity and muscle tone before and after phlebotomy procedures, while all of studied sample had a moderate motor stress during the same procedures. A statistical significant difference was found $(X^2 = 376.82, P = 0.000)$ as noted in Table (3).

Clearly, the majority of the subjects had mild behavioral stress as mild changes in crying, facial expression and sleep patterns before and after phlebotomy procedures (87.7% and 74.6% respectively). On the other hand, 78.5% of them had moderate behavioral stress during phlebotomy procedures and there was statistically significant difference (Table 4).

In Table (5) total neonatal stress was negatively correlated with hospitalization period and positively correlated with a diagnosis of newborn before phlebotomy procedures (r=-0.57 and r=0.86 respectively). These correlations were statistically significant (P = 0.000). Furthermore, total neonatal stress was positively

Table 1: The total percent scores of neonatal stress before, during and after phlebotomy procedures (n=130)

	Before		During	During		After			
Total neonatal stress	n=130	%	n=130	%	n=130	%	X^2	P value	
No stress	86	66.2%	0	0.0%	71	54.6%	150.207	0.000	
Mild stress	44	33.8%	114	87.7%	59	45.4%			
Moderate stress	0	0.0%	16	12.3%	0	0.0%			
Severe stress	0	0	0	0	0	0			

Table 2: The total percent scores of autonomic and physiological indicators of neonatal stress before, during and after phlebotomy procedures (n=130)

	Before		During		After			
Total Autonomic and Physiological Indicators	n=130	%	n=130	%	n=130	%	X^2	P value
No stress	82	63.1%	0	0.0%	83	63.8%	180.863	0.000
Mild stress	48	36.9%	91	70.0%	47	36.2%		
Moderate stress	0	0.0%	39	30.0%	0	0.0%		
Severe stress	0	0	0	0	0	0		

Table 3: The total percent scores of motor indicators of neonatal stress before, during and after phlebotomy procedures (n=130)

	Before		During		After			
Total Motor Indicators	n=130	%	n=130	%	n=130	%	X^2	P value
No stress	128	98.5	0	0	129	99.2	376.822	0.000
Mild stress	0	0	0	0	0	0		
Moderate stress	2	1.5	130	100	1	0.8		
Severe stress	0	0	0	0	0	0		

Table 4: The total percent scores of behavioral indicators of neonatal stress before, during and after phlebotomy procedures (n=130)

	Before		During		After			
Total Behavioral Indicators	n=130	%	n=130	%	n=130	%	X^2	P value
No stress	16	12.3%	0	0.0%	10	7.7%	204.544	0.000
Mild stress	114	87.7%	28	21.5%	97	74.6%		
Moderate stress	0	0.0%	102	78.5%	23	17.7%		
Severe stress	0	0	0	0	0	0		

Table 5: Correlations among neonatal demographic characteristics and total stress before, during, and after phlebotomy procedures (n=130).

		Total neonatal stress	Total neonatal stress				
Items		Before	During	After			
Hospitalization days	r	567	162	315			
	P value	.000**	.066	.000**			
Gestational age	r	.126	.065	.198			
	P value	.152	.461	.024*			
Weight /gram	r	.161	.003	.067			
	P value	.068	.969	.452			
Gender	r	026	042	049			
	P value	.767	.638	.578			
Delivery method	r	006	043	.060			
	P value	.948	.629	.497			
Diagnosis	r	.856	.396	.707			
	P value	.000**	.000**	.000**			
Feeding method	r	040	249	254			
	P value	.653	.004**	.004**			

^{**.} Correlation is significant at the 0.01 level (2-tailed).

^{*.} Correlation is significant at the 0.05 level (2-tailed).

correlated with his diagnosis and correlated negatively with feeding methods during phlebotomy procedures (r=0.39 and r=-0.25). These correlations were statistically significant (P=0.000 and P=0.004 respectively). Negative and statistically significant correlations were found between total neonatal stress and both hospitalization period and feeding methods after phlebotomy procedures (r=-0.32, P=0.000 and r=-0.25, P=0.004 respectively), while positive correlations were found between neonatal stress and both gestational age and his diagnosis after the same procedures (r=0.19 and r=0.71respectively). These correlations were statistically significant (P=0.02 and P=0.000 respectively).

DISCUSSION

All newborn infants, both full-term and preterm admitted to NICUs were exposed to a various invasive procedures, including venipuncture for diagnostic and medical reasons in the first 14 days of the neonatal admission. The use of behavioral and physiologic indicators is recommended for stress assessment in nonverbal patients [22, 23].

Neonate infants cannot verbalize their feeling of stress. They depend on pediatric nurses to assess their procedural pain or their feeling of distress to manage it well [24]. This assessment, includes observation of behavioral parameters as facial expressions, body movement and crying, as well as, evaluation of physiological parameters which include heart rate, respiration and blood pressure [25]. A study by Kenner and Wright [26] emphasized that gestational age affects newborns' pain response. Premature infants show fewer behavioral responses to pain. Newborns who were exposed to more frequent painful procedures in the NICU had decreased behavioral and increased physiological responses compared to newborns who experienced less number of painful procedures. According to Verklan and Walden [5] and Taksande et al. [12] who indicated that stressful events elevate preterm infant heart rate and blood pressure, while decreasing their oxygen levels. Also, environmental stimuli as simple touch, noise, bright light, can affect physiologic responses such as heart rate, respiration and oxygen saturation [27, 28]. These results are paralleled with the results of the present study which indicated that 92.3% of the present study sample has appropriate gestational age. They showed both behavioral and physiological responses, but, they were behaviorally more reactive to painful stimuli. This was explained by the fact that infants born preterm display altered pain thresholds and due to prematurity,

the nervous system is undeveloped, so preterm infant cannot express his feeling well regarding stress behaviorally compared with full-term infants. This was emphasized by a study of Grunau [29] and Ranger *et al.* [30] who emphasized that repeated untreated stressful events due to prematurity may cause alteration in behavioral developments.

The results of the present study confirmed that there was a statistically significant negative correlation between neonatal stress and hospitalization days before and after phlebotomy procedures. This finding could be related to around half of the study sample in the present study having a long period of hospitalization approximately 10-14 days, which in turn affect their responses to repeated painful experience. This is supported by the study of Grunau [29] and Ranger et al. [30] who concluded that repeated untreated stressful events may cause alteration in both brain and pain sensitivity in the future. Moreover, neonates exposed to NICU environmental stressors as equipment noises, bright lights and constant handling by pediatric nurses due to long hospitalization period can also threaten the neonatal body integrity and cause stress [31].

High risk neonates including preterm infants with very low birth weight and/or neonate infants who are suffering from respiratory distress and receiving nasal oxygen, or needing continuous positive airway pressure and ventilation support. In addition to, neonates with congenital anomalies, or sepsis and neonate infants of a diabetic mother are often exposed to a huge number of painful procedures, due to their medical conditions and their diagnosis, which in turn increase their stress in NICU [32]. This goes with the current study findings that revealed that neonatal stress was positively correlated with the diagnosis of newborn. This correlation was statistically significant.

Stress "Acts as a red flag for the perception of something threatening body integrity" [15]. Painful stimuli in neonate infant trigger stress responses, including cardiovascular, respiratory, immune, hormonal and behavioral changes. These physiological responses are followed by stress endocrine-metabolic reaction with hormones release as epinephrine, norepinephrine and cortisol. Moreover, hyperglycemia and lipid protein catabolism may result in, which alter preterm neonatal homeostatic balance [33, 34]. The current study findings showed that a positive correlation was found between gestational age of neonate infants and stress. This correlation was statistically significant. Conversely, a preterm neonate with gestational age of 28 and 29 weeks had more pain and suffering from

stress than those of 30 weeks or more gestational age. In NICU, preterm infants are exposed to several painful and stressful procedures which cause discomfort and stress and altered pain thresholds [35].

Regarding stress evaluation during painful procedures according to gender, it was observed that when a neonate is submitted to painful procedures and stressful situations as airway suction, venous puncture and intubation, male neonate had a higher percentage of severe pain as compared to female neonate [15]. Conversely, the findings of the present study showed that there was no correlation between stress of neonates and their gender and statistical difference was not found. This may referred to presence of painful procedures for long duration may affect the responding of newborns to stressful situations regardless their gender.

In the current study, neonatal stress was negatively correlated with feeding methods during and after phlebotomy procedures. This correlation was statistically significant as shown in the results of the present study. Breastfeeding is the best method to reduce pain in neonates undergoing a painful procedure. In a systematic review of 11 clinical trials, breast milk and breast feeding were shown to provide analgesia during procedural pain from venipuncture. Neonates given supplemental breast milk had a significantly less increase in the heart rate and behavioral pain scores. Furthermore, the duration of crying time and oxygen saturation decrease in study group compared with the control group. In short, breast feeding has been consistently associated with a reduction on behavioral pain response and improvement in physiological stability [36].

The results showed that more than two thirds of the sample had no autonomic and physiological indicators, as change in heart rate, blood pressure, respiration, oxygen saturation and skin color of neonatal stress before and after phlebotomy procedures compared to 70% of the sample had a mild degree of autonomic and physiological stress during these procedures with a statistically significant difference. This may explained by frequent painful procedures were performed often with inadequate pain management. Neonatal stresss may depends on duration and type of stimulus. neonate clinical factors, or organizational factors. Moreover, this variation may due to physiological immaturity, or this stress may unrelated to the painful procedure. Also, they can occur with fear, infants' disease and discomfort. The responses may also be altered by the physiological state of the baby immediately preceding the painful stimulus, such as the stage of wakefulness, duration since last feed, restraint techniques used[15].Clearly, the majority of the subjects had mild behavioral stress as mild changes in crying, facial expression and sleep patterns before and after phlebotomy procedures. On the other hand, 78.5% of them had moderate behavioral stress during phlebotomy procedures and there was a statistically significant difference. This may explain by the fact that behavioral changes were directly associated with pain intensity during the painful procedure.

The majority of newborn infants did not have any motor indicators of stress as a change in neonatal activity and muscle tone before and after phlebotomy procedures, while all of studied sample had moderate motor stress during the same procedures. A statistical significant difference was found. This may be related to painful experiences have many parameters as biological, psychological and social, when examining pain expression, as well as, the newborn infant displays a hypersensitivity to sensory stimuli and as such, is more prone to pain and its consequences. In this sense, Derebent and YiDit [37] indicated that there are many factors affecting stress responses of neonate undergoing phlebotomy. These factors include: gestational age of infant, his gender, state of wakefulness, painful stimulus type, length and general health condition, type of birth, severity of illness, past experience of neonate, individual differences and coping skills.

In short, painful experience in neonate infants has later consequences in the short term and long term as well. Appropriate assessment and management of stress is necessary to develop nursing care plans to improve infants' health and prevent adverse effects of those stressors.

CONCLUSION

In the light of the current study findings, it is concluded that the majority of newborn infants suffered from stress during phlebotomy procedures as assessed by physiological, autonomic, motor and behavioral indicators, while neonate infants did not have any change in physiological, autonomic and motor indicators of stress before and after phlebotomy, except behavioral indicators. Motor indicators which include activity and overall tone of the neonate infants showed the highest percentage of neonatal stress during phlebotomy procedures. There were statistically significant differences among physiological, autonomic, motor and behavioral indicators and total stress for neonate infants undergoing phlebotomy procedures.

Recommendations: Based on the findings of this study, the following recommendations are suggested:

- An educational training program on non-pharmacological methods for pediatric nurses in NICU to reduce stress for neonate undergoing phlebotomy procedures.
- Periodical evaluation of neonatal stress in NICU is recommended to determine the appropriate strategies for minimizing stress for neonate undergoing phlebotomy procedures.
- Further research studies are needed regarding effective non-pharmacological methods to alleviate procedural stress, and identifying factors affecting it for neonate undergoing phlebotomy procedures.

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REFERENCES

- Basavanthappa, B.T., 2015. Child Health Nursing. New Delhi, India: Jaypee brothers Medical, Chapter (8). Neonatal Nursing (Normal)., pp: 251.
- Merriam Webster's Collegiate Dictionary, 1994. Phlebotomy. (10th ed.). Springfield: Merriam-Webster, pp: 1164.
- Clark, M., M. Bond and J. Hecker, 2007. Environmental stress, psychological stress and allostatic load. Psychology, Health & Medicine, 72(1): 18-30.
- Alexa, O., F. Kim and P. Lori, 2017. Does music positively impact preterm infant outcomes? Advances in Neonatal Care, 17(3): 192-202. DOI: 10.1097/ANC.0000000000000394.
- Verklan, M.T. and M. Walden, 2015. Core curriculum for neonatal aimtensive care nursing. (5th ed.). Texas: Saunders Co, Chapter (16). Pain Assessment and Management, pp. 316-329.
- Newnham, C.A., T.E. Inder and J. Milgrom, 2009. Measuring preterm cumulative stressors within the NICU: The neonatal infant stressor scale. Early Hum Dev., 85(9): 549-555.

- Smith, G.C., J. Gutovich, C. Smyser, R. Pineda, C. Newnham, T.H. Tjoeng, C. Vavasseur, M. Wallendorf, J. Neil and T. Inder, 2011. Neonatal intensive care unit stress is assosciated with brain development in preterm infants. Ann Neurol., 70(4): 541-549.
- 8. Huang, X., L. Li, J. Zhou, F. He, C. Zhong and B. Wang, 2018. Evaluation of three pain assessment scales used for ventilated neonates. J. Clin Nurs., 27(19-20): 3522-3529. doi: 10.1111/jocn.14585.
- National Cancer Institute at the National Institutes of Health: U.S. Department of Health and Human Services, 2018. Definition of phlebotomy. Available at: https://www.cancer.gov/publications/ dictionaries/ cancer-terms/ def/phlebotomy.
- Kapellou, O., 2011. Blood sampling in infants (reducing pain and morbidity). BMJ Clin Evid, 2011: 0313.
- Pourashoori, Z., K. Mirnia, F. Ghorbani, A. Safaiyan, M. A. Nematzadeh and M.A. Bostanabad, 2018. Effect of blood sampling site on the changes in the physiological indices of preterm infants: A crossover clinical trial. IJN, 9(3): 42-48. DOI: 10.22038/ijn.2018.27487.1366.
- Taksande, A.M., M. Jain, K.Y. Vilhekar and D. Chitre, 2005. Pain response of neonates to venipuncture. Indian J. Pediatr, 72(9): 751-3. DOI: 10.1007/BF02734146.
- King, T.L., C. Mary, M.C. Brucker, K. Osborne, C.M. Jevitt, 2019. Varney's Midwifery. (6th ed.). Sudbury, US: Jones and Bartlett Publisher, Chapter (7). Principles of Pain Management, pp: 52-63.
- 14. Akcan, E., R. Yiğit and A. Atıcı, 2009. The effect of kangaroo care on pain in premature infants during invasive procedures. Turk J. Pediatr, 51: 14-18.
- Cruz, C.T., J.S. Gomes, R.M. Kirchner and E.M. Stumm, 2016. Evaluation of pain of neonates during invasive procedures in intensive care, Rev. dor, 17(3): 197-200. http://dx.doi.org/10.5935/1806-0013.20160070.
- Vinall, J., S.P. Miller, V. Chau, S. Brummelte, A.R. Synnes and R.E. Grunau, 2012. Neonatal pain in relation to postnatal growth in infants born very preterm. Pain, 153(7): 1374-81. doi: 10.1016/j.pain.2012.02.007.

- 17. Doesburg, S.M., C.M. Chau, T.P. Cheung, A. Moiseev, U. Ribary, A.T. Herdman, S.P. Miller, I.L. Cepeda, A. Synnes and R. E. Grunau, 2013. Neonatal pain-related stress functional cortical activity and visual-perceptual abilities in school-age children born at extremely low gestational age, Pain, 154: 1946-52.
- 18. Brummelte, S., C.M. Chau, I.L. Cepeda, A. Degenhardt, J. Weinberg, A.R. Synnes and R.E. Grunau, 2015. Cortisol levels in former preterm children at school age are predicted by neonatal procedural pain-related stress. Psychoneuroendocrinology, 51: 151-163.
- Modrcin-McCarthy, M.A., S. McCue and J. Walker, 1997. Preterm infants and stress: A tool for the neonatal nurse. J. Perinatal & Neonatal Nursing, 10(4): 62–71
- Abd El-motalib, M., 2008. Assessment of stress in premature neonates during blood sampling procedure, M. S. thesis, Cairo Unive., Faculty of Nursing. Cairo, Egypt.
- Hassan, A., 2018. Effect of tactile stimulation on neonatal stress during invasive procedures at Neonatal Intensive Care Units in Port Said, M. S. thesis, Port Said Unive., Faculty of Nursing. Port-Said, Egypt.
- 22. Kappesser, J., J. De Laffolie, E. Kamper, D. Faas, H. Ehrhardt, L.S. Franck and C. Hermann, 2019. Pain-specific reactions or indicators of a general stress response? Investigating the Discriminant Validity of Five Well-established Neonatal Pain Assessment Tools. Clin Pain, 35(2): 101-110. DOI: 10.1097/AJP.00000000000000660
- Arbour, C. and C. Gélinas, 2014. Behavioral and physiologic indicators of pain in nonverbal patients with a traumatic brain injury: an integrative review. Pain Manag Nurs, 15(2): 506-18. doi: 10.1016/j.pmn.2012.03.004.
- 24. Devsam, B., 2017. Clinical guidelines nursing: Neonatal pain assessment. The Royal Children's Hospital (RCH): Malbourne. Available at: https://www.rch.org.au/rchcpg/hospital_clinical_g uideline index/Neonatal Pain Assessment/
- Hall, R. and K.J. Anand, 2014. Pain management in newborns. Clin Perinatol, 41: 895-924. http://dx.doi.org/10.1016/j.clp.2014.08.010
- Kenner, C. and J.L. Wright, 2014. Comprehensive neonatal nursing care. (4th ed.). New York, NY: Springer Co. Chapter (23). Pain in the Newborn and Infant, pp: 571-568.

- 27. Smith, J.R., 2012. Comforting touch in the very preterm hospitalized infant: an integrative review. Adv. Neonatal Care, 12(6): 349-365.
- Mangat, A.K., J.O. Chen, K.I. Quah-Smith and G.M. Schmölzer, 2018. A Review of Nonpharmacological treatments for pain management in newborn infants. Children, 5: 130. doi:10.3390/ children5100130.
- Grunau, R.E., 2013. Neonatal pain in very preterm infants: Long term effects on brain, neurodevelopment and pain reactivity. Rambam Maimonides Med. J. Oct 29, 4(4): e0025. doi: 10.5041/RMMJ.10132.
- Ranger, M., C.M. Chau, A. Garg, T.S. Woodward, M.F. Beg, B. Bjornson, K. Poskitt, K. Fitzpatrick, A.R. Synnes, S.P. Miller and R.E. Grunau, 2013. Neonatal pain-related stress predicts cortical thickness at age 7 years in children born very preterm. PLoS one, 8(10): e76702.
- 31. Warren, I., 2002. Facilitating infant adaptation: The nursery environment. Semin Neonatol, 7(6): 459-67 7. DOI: 10.1053/siny.2002.0151.
- 32. Levy, J. and A.E. D'Harlingue, 2013. Recognition, Stabilization and Transport of the High-Risk Newborn, 71(103): 83-84.
- Lissauer, T., A. Fanaroff, L. Miall and J. Fanaroff, 2016. Neonatology at a glance. (3rd ed.). John Wiley & Sons. Part (8). Aspects of neonatal intensive care, pp: 148-168.
- 34. Santos, L.M., M.P. Pereira, L.F. Santos and R.C. Santana, 2012. Avaliação da dor no recémnascido prematuro em Unidade de Terapia Intensiva. Rev. Bras Enferm, Brasilia, 65(1): 27-33.
- 35. Lickliter, R., 2011. The integrated development of sensory organization. Clinical Perinatology, 38(4): 591-603.
- Reece-Stremtan, S., L. Gray and the Academy of Breastfeeding Medicine, 2016. ABM Clinical Protocol #23: Nonpharmacological management of procedure-related pain in the breastfeeding infant. BREASTFEEDINGMEDICINE, 11(9): 425-428. DOI: 10.1089/bfm.2016.29025.srs
- Derebent, E. and R. YiĐĞit, 2008. Non-parmacological pain management in newborn. Turk J. Pediatr, 22(2): 113-118. Available at: http://www.fusabil.org.