

Investigation of the Relationship Between Neuromotor Behavior and Pain, Comfort, Apgar Score and Clinical Factors in Premature Neonates

Prematüre Yenidoğanda Ağrı, Konfor, Apgar Skoru Ve Klinik Özelliklerin Nöromotor Davranışına İlişkisinin İncelenmesi

Erdoğan KAVLAK¹, Fatih TEKİN², Mustafa BURAK³

¹ Assoc. Prof., Pamukkale University, School of Physical Therapy and Rehabilitation, Denizli, Turkey

² PT MSc., Pamukkale University, School of Physical Therapy and Rehabilitation, Denizli, Turkey

³ PT MSc., Gazi University, Faculty of Health Sciences, Physiotherapy and Rehabilitation Department, Ankara, Turkey

ABSTRACT

Purpose: Abnormalities detected by neurological examinations and developmental tests performed in premature infants can be transient or severe enough to affect the survival of a baby. Aim of this study was to investigate the relationship between neuromotor behavior and pain, comfort, Apgar Score and clinical factors in premature neonates. **Material and Methods:** 13 neonates, (M:6, F:7) who were being treated for prematurity diagnosis, were included in study. A clinical data form, pain assessment, comfort evaluation for pain and stress, Apgar Score and neuromotor skills assessment were performed to neonates. **Results:** Presence of maternal psychological stress during one-year period before birth of baby and male gender caused retardation in terms of neuromotor behavior ($p=0,038$). Infants whose respiration depends on an inhaler are the worst in neuromotor behavior ($p=0,023$). There was a positive correlation between neuromotor behavior skills of premature neonate and duration of pregnancy and birth weight, and negative correlation with pain and comfort status ($p=0,042$). There was no correlation between Apgar Score and neuromotor behavior ($p=0,016$). **Discussion:** Presence of maternal psychological stress, male gender, using respiratory device, pain and worse comfort status adversely affect neuromotor skills. Conversely, breastfeeding, longer duration of pregnancy period, and higher birth weight positively affect neuromotor skills. There is no relationship between neuromotor skills and Apgar Score; neuromotor skills and delivery method.

Keywords: Behavior; Premature; Pain; Patient Comfort; Apgar Score

ÖZ

Amaç: Prematüre infantlarda nörolojik muayeneler ve gelişimsel testlerle tespit edilen anormallikler, geçici veya bebeğin yaşamını etkileyebilecek kadar ciddi olabilir. Bu çalışmanın amacı, prematüre yenidoğanlarda nöromotor davranış ile ağrı, konfor, Apgar Skoru ve klinik özellikler arasındaki ilişkiyi araştırmaktır. **Gereç ve Yöntem:** Çalışmaya prematürite tanısı ile tedavi gören 13 yenidoğan ($E=6$, $K=7$) dahil edildi. Olgulara klinik bilgi formu dolduruldu ve ağrı değerlendirmesi, ağrı ve stresse dayalı konfor değerlendirmesi, Apgar Skoru ve nöromotor davranış değerlendirme yapıldı. **Sonuçlar:** Bebeğin doğumundan önceki 1 yıllık dönemde maternal psikolojik stresin varlığının ve bebeğin erkek cinsiyette olmasının, nöromotor davranışların gelişiminde gecikmelere neden olduğu görülmüştür ($p=0,038$). Solunum cihazına bağlı olarak respirasyon yapabilen infantlar, nöromotor davranış bakımından en kötü durumdadır ($p=0,023$). Prematüre yenidoğanın nöromotor davranış becerileri ile hamilelik süresi ve doğum ağırlığı arasında pozitif; ağrı ve konfor durumu ile ise negatif bir korelasyon mevcuttur ($p=0,042$). Nöromotor davranış becerileri ile Apgar Skoru arasında ise herhangi bir ilişki bulunamamıştır ($p=0,016$). **Tartışma:** Maternal psikolojik stresin varlığı, erkek cinsiyet, solunum cihazına bağlı solunum, ağrı varlığı ve daha kötü konfor durumu nöromotor becerileri olumsuz yönde etkiler. Buna karşılık emzirme yoluyla beslenme, daha uzun gebelik süresi ve daha yüksek doğum ağırlığı nöromotor becerileri olumlu yönde etkiler. Nöromotor beceriler ile Apgar Skoru ve doğum yöntemi arasında ise ilişki yoktur.

Anahtar Kelimeler: Davranış; Prematüre; Ağrı; Hasta Konforu; Apgar Skoru

Sorumlu Yazar (Corresponding Author): Erdoğan KAVLAK E-mail: kavlake@hotmail.com

ORCID ID: 0000-0002-6344-259X

Geliş Tarihi (Received): 14.02.2019; Kabul Tarihi (Accepted): 31.10.2019

The normal gestation period is the period from the first day of the mother's last menstruation to delivery. This period lasts 40 weeks and may range from 37 to 42 weeks. Neonate babies are divided into three groups as preterm, term and postterm according to the gestational week. Neonates born in term are the babies who were born by completing this period (Can and İnce, 2002).

Those born before 37 weeks of gestation are considered to be preterm or premature, and those who complete 42 weeks of age are considered to be postterm or postmature. The "premature baby" phrase refers to babies born between 23 weeks of gestation and 36 weeks of gestation + 6 days. Premature infants are divided into groups according to gestational ages and birth weights: born between 23 and 27 weeks are extreme premature; 27 and 34 weeks are moderately premature; 34 and 37 weeks are considered to be premature at the border. Less than 2500 gr of birth weight is named as low birth weight; below 1500 gr as very low birth weight; below 1000 gr as an extremely low birth weight (Can et al., 2002).

Recent advances in the medical and technological fields have increased the quality of neonatal intensive care units (NICUs) and many premature infant incubator technologies have been started to be kept alive by discussing the viability limits (Dağoğlu, Yurdakök and Erdem, 2004). However, in 50% of the living babies, neurodevelopmental disorders including attention deficit, motor incoordination, muscle tonus disorders, motor developmental delay, cognitive disorders and developmental problems, mild developmental disorders in 20-25% and cerebral palsy in 5-15% (Celik 2018, Çelik 2018, Noble and Boyd, 2012; Woodward, Anderson, Austin et al., 2006). Abnormalities detected by neurological examinations and developmental tests performed in premature infants can be transient or severe, which may be severe enough to affect the survival of the baby.

In the current literature, there is no study examining the relationship between neuromotor behavior and pain, comfort, Apgar score, gender, respiratory status, maternal stress, delivery method, birth weight, duration of pregnancy in premature infants at a glance. Aim of this study was to investigate the relationship between neuromotor behavior and pain, comfort, Apgar Score and clinical factors in premature neonates.

MATERIAL AND METHODS

The study was performed in the Neonatal Intensive

Care Unit of Pamukkale University Hospital between January 2018 and September 2018 with 13 neonates who were treated for prematurity diagnosis (M:6, F:7) and their mothers with the permission of parents by written consent forms. All assessments made by specialist physiotherapists. During the study process, the Helsinki Declaration was adopted. Criteria for infants inclusion in the study;

- diagnosis of prematurity
- no additional disease
- absence of surgical history
- was not currently using analgesic drugs.

The demographic and clinical data including Apgar Score were obtained from the patient files. Neonatal Infant Pain Scale (NIPS) for pain assessment, Premature Infant Comfort Scale (PICS) for comfort evaluation for pain and stress, and Neonatal Neuromotor Behavioural Assessment (NNBA) was used to evaluate neuromotor skills.

Clinical Data Form

The first 3 months of pregnancy and general maternal psychological stress in the last 1 year, and the duration of pregnancy, gender, birth weight, delivery method, length of stay in neonatal intensive care unit, respiratory rate, feeding style and surgical history were recorded in the clinical data form.

Neonatal Infant Pain Scale

Lawrence et al. developed a six-point NIPS based on the results of 43 experienced neonatal nurses working at the Eastern Ontario Children's Hospital. Nurses were asked to describe the levels of pain and stress-related behavior at varying levels in premature and term babies responding to painful stimulus. Nurses defined six types of behavioral categories in this population: facial expression, crying, breathing patterns, arm movement, leg movement, and vigilance. There are three categories of crying (0, 1, 2); two of all other behaviors (0, 1). The total score ranged from 0 to 7 and the higher score indicates a higher pain (Lawrance, Alcock, McGrath et al., 1993). Turkish validity and reliability study of the scale was not performed.

Apgar Score

Dr. Virginia Apgar developed a scoring system in 1952 to assess the clinical status of the neonate in the first minute and to determine the urgent need for respiratory intervention.

The second study, which examined more patients, was published in 1958. This scoring system

allowed the standard evaluation of infants after birth. The Apgar Score consists of five components, each with a score of 0, 1 and 2; 1) color; 2) heart rate; 3) reflexes; 4) muscle tone and 5) respiration. Apgar Score determines the clinical symptoms of the neonatal such as cyanosis, pallor, bradycardia, reduced reflex responses to stimulus, hypotonia, and apnea. This score is calculated every 5 minutes for babies with a score less than 7 and 20 minutes for babies with a score lower than 7 after birth. The Apgar Score is an accepted and usable method for assessing the state of the neonate immediately after birth and in response to stimulation; however, it has been improperly used in neurological outgrowth (The Apgar Score, 2015).

Premature Infant Comfort Scale

Ambuel et al. (Ambuel, Hamlett, Marx et al., 1992) developed the comfort scale to measure the pain and stress levels of 0-18 year-old children in pediatric intensive care unit, then Monique et al. in 2007 (Monique, Caljouw-Marguerite, Kloos-Madeleine et al., 2007) adapted it to premature babies whose age ≥ 28 and ≤ 37 weeks. PICS is a multidimensional scale which is used to evaluate comfort and pain behaviorally and psychologically. PICS is used to evaluate 7 parameters such as Awakening, Calmness/Agitation, Respiratory Status (only with mechanical ventilation support) or Crying (not evaluated only for children with spontaneous breathing), Physical Movement, Muscle Tonus, Face Movement and Average Heart Rate. Each item is a 5-point Likert type that is scored from bad to good. According to PICS, the comfort of the baby is evaluated on the total score. Accordingly, it shows 35 lowest and 7 highest comfort points. The high score obtained from the scale indicates that the comfort level is low. The total score of ≥ 17 is the cut-off value of the scale which is the limit value for the comfort level of the baby and shows that there is a need for a pain-reducing intervention (Monique et al., 2007). There is validity and reliability study of the scale in Turkish (Küçük Alemdar & Güdücü Tüfekci, 2015).

Neonatal Neuromotor Behavioural Assessment

The assessment is subdivided into four sections: neurological items, behavioural items, autonomic items, and motor functions with scoring on a point system from 0 to 4. Zero and 1 record the worst possible responses while 2, 3 and 4 record better to

best responses respectively. For ease of interpretation, total scores for each parameter were categorised into one of three groups: abnormal, suspect or normal. These anticipated developmental categories were derived from the assessment by considering the scores allocated to each functional area. Generally, scores of 0 or 1 were considered to be abnormal; scores of 2, suspect; and scores of 3 or 4 normal. The exception was with stability of vital signs, where a score of 0 was considered abnormal, 1 suspect and 2 normal (Carmichael, Burns, Gray et al., 1997). Turkish validity and reliability study of the scale was not performed.

Statistical Analysis

When 12 patients were included in the study as the result of the power analysis performed, 95% confidence was calculated to reach 90% confidence. The data were analyzed by SPSS packet program. Continuous variables were given as mean \pm standard deviation and categorical variables as number and percentage. Spearman correlation coefficients were used for correlation analysis of data that does not have a normal distribution. The Pearson Chi-Square test was used to measure the relationship between categorical variables.

RESULTS

Table 1 and Table 2 show the categorical distribution of the clinical data of the patients included in the study. Table 2 also shows the mean and minimum-maximum values of NNBA, Apgar, NIPS and PICS scores and Table 3 shows the categorical distributions.

Table 4 shows the distribution of the clinical conditions of the cases to the levels of neuromotor behavior with together the significance values of the distributions.

According to this, the presence of psychological stress in the mother during the one-year period before the birth of the baby caused retardation in terms of neuromotor behavior ($p=0,038$). In the same way, the male gender is also retards in terms of neuromotor behavior ($p=0,01$). Infants whose respiration is depending on the inhaler are the worst in neuromotor behavior and infants who could make unassisted respiration are in the best condition ($p=0,023$).

Table 1. Categorical distribution of clinical data

Clinical Data		n	%
Maternal stress in the first trimester	Yes	6	46.2
	No	7	53.8
Maternal stress throughout pregnancy	Yes	7	53.8
	No	6	46.2
Maternal stress in the last 1 year	Yes	7	53.8
	No	6	46.2
Gender	Boy	6	46.2
	Girl	7	53.8
Delivery method	Normal	2	15.4
	Cesarean	11	84.6
Respiratory status of the neonate	Depending on the inhaler	2	15.4
	Oxygen support in the incubator	4	30.8
Nutritional status of the neonate	Unassisted	7	53.8
	Breastfeeding	8	61.5
	Nasogastric tube	1	7.7
	Mixed	4	30.8

Table 2. Mean and minimum-maximum values of clinical data and NNBA, Apgar, NIPS and PICS scores

	X ± SD	Minimum	Maximum
Duration of pregnancy (weeks)	29.77±4.14	23	36
Birth weight (gr)	1448±742	520	2900
Length of stay in NICU (days)	71±63	5	188
NNBA	32.77±9.88	17	52
NIPS	2.38±2.1	0	6
PICS	15.77±2.48	14	21
Apgar 1st min	5.38±1.12	3	7
Apgar 5th min	7±1.08	5	9
Apgar 10th min	7.92±0.76	7	9

NICU: Neonatal Intensive Care Unit **NNBA:** Neonatal Neuromotor Behavioural Assessment **NIPS:** Neonatal Infant Pain Scale **PICS:** Premature Infant Comfort Scale

Table 3. Categorical distribution of Apgar, NIPS, PICS and NNBA scores

		n	%
Apgar 1st min.	Resuscitation	1	7.7
	Ventilation	12	92.3
	Normal	0	0
Apgar 5th min.	Resuscitation	0	0
	Ventilation	9	69.2
	Normal	4	30.8
Apgar 10th min.	Resuscitation	0	0
	Ventilation	4	30.8
	Normal	9	69.2
NIPS	Pain (-)	8	61.5
	Pain (+)	5	38.5
PICS	Good	10	76.9
	Bad	3	23.1
NNBA	Abnormal	3	23.1
	Suspicious	6	46.2
	Normal	4	30.7

NNBA: Neonatal Neuromotor Behavioural Assessment **NIPS:** Neonatal Infant Pain Scale **PICS:** Premature Infant Comfort Scale

Table 4. Distribution of clinical cases to neuromotor behavior levels

			NNBA			p
			Abnormal	Suspicious	Normal	
			n	n	n	
Maternal stress in the first trimester	Yes	n	3	3	0	0.303
		%	0	50	50	
	No	n	0	3	4	
		%	0	42.8	57.2	
Maternal stress throughout the pregnancy	Yes	n	3	4	0	0.321
		%	42.8	57.2	0	
	No	n	0	2	4	
		%	0	33.3	66.7	
Maternal stress in the last 1 year	Yes	n	3	4	0	0.002*
		%	42.8	57.2	0	
	No	n	0	2	4	
		%	0	33.3	66.7	
Gender	Boy	n	3	2	1	0.044*
		%	50	33.3	16.7	
	Girl	n	0	4	3	
		%	0	57.2	42.8	
Delivery Method	Normal	n	0	1	1	0.391
		%	0	50	50	
	Cesarean	n	3	5	3	
		%	27.3	45.4	27.3	
Respiratory status of the neonate	Depending on the inhaler	n	3	2	0	0.049*
		%	60	40	0	
	Oxygen support in the incubator	n	0	3	1	
		%	0	75	25	
Nutritional status of the neonate	Unassisted	n	0	1	3	0.363
		%	0	25	75	
	Breastfeeding	n	0	1	4	
		%	0	20	80	
	Nasogastric tube	n	3	0	0	
		%	100	0	0	
	Mixed	n	0	5	0	
		%	0	100	0	

Chi-Square Test NNBA: Neonatal Neuromotor Behavioural Assessment *: p<0.05

Table 5 shows the correlation of duration of pregnancy, birth weight, length of stay in NICU, pain status, comfort status, and Apgar scores with neuromotor behavior.

According to this, there is a statistically significant and positive moderate correlation between the neuromotor behavior skills of premature neonate and

duration of pregnancy and birth weight; while there is a statistically significant and negative correlation with the pain and comfort status ($p=0.042$). There is no correlation between the Apgar Score at 1st, 5th and 10th minutes and neuromotor behavior during the NICU staying period ($p=0.016$).

Table 5. Correlation of duration of pregnancy, birth weight, length of stay in NICU, pain status, comfort status, and Apgar scores with neuromotor behavior

	Duration of Pregnancy	Birth Weight	Length of Stay in NICU	NIPS	PICS	Apgar Score		
						1st min	5th min	10th min
NNBA	r	0.488	0.453	-0.175	-0.480	-0.460	0.181	0.075
	p	0.039	0.048	0.400	0.045	0.039	0.033	0.039

Spearman Correlation Analysis **NICU**: Neonatal Intensive Care Unit **NNBA**: Neonatal Neuromotor Behavioural Assessment **NIPS**: Neonatal Infant Pain Scale **PICS**: Premature Infant Comfort Scale

DISCUSSION

In this study that we carried out in premature newborns, the factors such as the presence of maternal psychological stress during the pregnancy, duration of pregnancy, the low birth weight, the male gender, the respiration due to respiratory devices in the NICU, feeding apart from her mother and the pain of neonate were found to affect neuromotor skills negatively.

It was observed that the longer pregnancy duration, the higher birth weight, breastfeeding, the respiration was performed spontaneously and the female gender affected the neuromotor behavior of the neonate positively.

It was also found that there was no relationship between neuromotor behaviors and delivery method and between neuromotor behaviors and the Apgar Score.

Neuromotor behavior of the babies whose mothers are stressed in the pre-pregnancy period, the first trimester of pregnancy which is very important in terms of the neonate's neurological development, and the whole pregnancy period are retarded compared to the other babies.

There is strong evidence in a review showing that there is a direct link between prenatal anxiety/stress and fetal behavior observed with ultrasound from postmenstrual 27-28 weeks. Likewise there is evidence about a link between maternal mood and a child's long-term behavior in pregnancy period (Van den Bergh, Mulder, Mennes et al., 2005).

Recently, it has been suggested that prenatal stress has a direct effect on fetal brain development independent of its effect on birth weight (Graignic-Philippea, Dayan, Chokronb et al., 2014).

Neuroscience studies show that the hippocampus is affected by the stress of early development (Francis, Diorio, LaPlante et al., 1996).

Hippocampal pyramidal neurons contain high concentrations of glucocorticoid receptors sensitive to severe stress-induced hypercortisolism or exposure to exogenous glucocorticoids (Gunnar, 1998). In infancy and childhood, overproduction of glucocorticoids and excessive HPA activity negatively affect neurodevelopment, emotional regulation, and intellectual development (Gunnar, 1998). Studies highlighting neuropsychological deficiencies such as motor problems, poor attention/concentration, poor social/emotional development, decreasing balance, and discovery behaviors all point to neurodevelopmental problems (Schneider, 1992; Schneider and Coe, 1993).

Premature neonate girls are better than boys in terms of neuromotor behavior. Reason of this situation, it has been thought that the girl infants may be more resistant to negativities affecting neuromotor behavior.

It has been reported that male gender has a disadvantage as one of the many other risk factors associated with neurodevelopmental outcomes in preterm babies (Vohr, Wright, Dusick et al., 2004; Hack, Wilson Costello, Friedman et al., 2000; Wood, Costeloe, Gibson et al., 2005; Wood, Marlow, Costeloe et al., 2000; Hoekstra, Ferrara, Couser et al., 2004; Msall, Buck, Rogers et al., 1993; Hindmarsh, O'Callaghan, Mohay et al., 2000).

The fact that the neonate was born with normal vaginal delivery or by cesarean section did not have a significant effect on neuromotor skills. Although with the normal vaginal delivery, the neonate's brain is more likely to be exposed to anoxia compared to delivery by cesarean section, it is understood that the delivery method does not affect neuromotor skills unless difficult birth is concerned.

Premature neonates who could perform non-assisted respiration are better in terms of neuromotor skills compared to babies who receive oxygen support into the incubator and are dependent on the respiratory device, respectively. This is probably due to the more common and more severe brain damage of infants who cannot breathe without the device. In addition, the movements of babies who are dependent the respiratory device are more limited than other babies. Neuromotor skills of infants with less mobility in the incubator are also lower.

Neuromotor skills of premature neonates who fed by breastfeeding are better than the neonates who by mixed type and the neonates by nasogastric catheters, respectively. The sucking reflex of the breastfed neonates the have more developed neuromotor behaviors. The neonates who can only be fed by nasogastric catheterisation have retarded neuromotor behaviors compared to the others, because of their neurological deficits.

There is a positive correlation between the neuromotor behavior of premature neonate and duration of pregnancy and birth weight. Neonates who born after a longer duration of pregnancy and therefore have a higher birth weight have completed their neurological development to a greater extent and thus their neuromotor behavior is more developed. Neurological development of neonates born earlier and with less birth weight are retarded.

Pain and comfort status of premature neonate is closely related to neuromotor skills. The neuromotor

behaviors of the infants who are less painful and have higher levels of comfort related to pain and stress are also better. This situation was thought to be caused by the movement avoidance behavior due to the increase of the pain and hence the stress of the neonates with pain and stress.

Neonatal acute painful experiences negatively affect brain development results during neurobehavioral and postnatal growth, cortical activation, corticospinal development, and NICU hospitalizations of preterm babies. Further, the possible effects of pain-related stress events or healing on painful stimuli on the development of preterm newborns were detected at different ages, indicating early adverse effects (Monique et al., 2007).

There was no correlation between length of stay in NICU and neuromotor skills of premature neonate. The age of the neonate increases as the length of stay in NICU increases, so the neuromotor skills are expected to increase. Similarly, the neonate who needs to stay longer in NICU may also be considered to have retarded neurological development. Therefore, it is thought that there is no relationship between these two parameters.

There is no relationship between neuromotor skills and Apgar Score. Although there is a widespread understanding in the literature that the Apgar Score may give an idea about possible neurological problems, the results of the present study and the Virginia Apgar's views who developed The Apgar Score do not confirm this understanding (Score A, 1986; The Apgar Score, 2015).

The 5-minute Apgar score in infants shows weak correlation with future neurological outcomes. For example, a score between 0 and 3 in 5 minutes was associated with a slightly increased cerebral palsy risk compared to higher scores. Inversely, 75% of children with cerebral palsy had normal scores in 5 minutes (Nelson and Ellenberg, 1981).

Limitations of this study were, if a larger number of cases could be included in the study, some statistics could be more efficient. A subjective assessment was used when examining the maternal stress, instead of an objective assessment. Long-term follow-up and the presence of a control group made the results of the study more valuable.

In conclusion, presence of maternal psychological stress in the 3-month period before pregnancy, the first trimester of pregnancy, and the whole pregnancy period adversely affect the neuromotor skills of the premature neonate. Premature neonate girls are better than the boys in

terms of neuromotor behavior. The fact that the baby is born with normal vaginal delivery or by caesarean section has no significant effect on neuromotor skills. Neuromotor behavior of premature neonates who could only respirate depending on the respiratory device is much lower than those that could breathe independently of the device. The breastfed neonates are better than the others in terms of neuromotor skills. Neuromotor skills of premature neonates born after a longer duration of pregnancy period and higher birth weight are better. Pain and comfort status of premature neonates and neuromotor behavior are closely related. Neuromotor behaviors of premature neonates with more severe pain and worse comfort are also worse. There is no relationship between neuromotor skills and Apgar Score.

References

- Alemdar, D. K., & Tufekci, F. G. (2015). The reliability and validity of the premature infant comfort scale's Turkish/Premature bebek konfor ölçüğünün Türkçe geçerlilik ve güvenilirliği. *HEAD*, 12(2), 142-149.
- Ambuel, B., Hamlett, K.W., Marx, C.M., & Blimer, J.L. (1992). Assessing distress in pediatric intensive care environments: The COMFORT Scale. *J Pediatr Psychol*, 17, 95-109.
- Can, G., Neyzi, O., & Ertuğrul, T.Y. (2002). Preterm doğanlar, intrauterin büyümeye geriliği. İstanbul, Nobel Matbaacılık, 326-334.
- Carmichael, K., Burns, Y., Gray, P., & O'Callaghan, M. (1997). Neuromotor behavioural assessment of preterm infants at risk for impaired development. *Aust J Physiother*, 43(2), 101-107.
- Celik, H. İ., Elbasan, B., Gucuyener, K., Kayihan, H., & Huri, M. (2018). Investigation of the relationship between sensory processing and motor development in preterm infants. *Am J Occup Ther*, 72(1), 7201195020p1-7201195020p7.
- Çelik, H. İ., Elbasan, B., Güçüyener, K., Kayihan, H., & Meral, H. (2018). Preterm ve Term Bebeklerde Duyusal İşlemleme Becerisinin İncelenmesi. *Turk J Physiother Rehabil* 29(2), 31-36.
- Dağoğlu, T., Yurdakök, M., & Erdem, G. (2004). Neonatoloji'de Prematürite, Ankara, Güneş Tip Kitapları, 123-129.
- Francis, D., Diorio, J., LaPlante, P., Weaver, S., Seckl, J.R., & Meaney, M.J. (1996). The role of early environmental events in regulating neuroendocrine development. Moms, pups, stress, and glucocorticoid receptors. *Ann N Y Acad Sci*, 794, 136-152.
- Graignic-Philippe, R., Dayan, J., Chokronb, S., Jacquetb, A.Y., & Tordjmana, S. (2014). Effects of prenatal stress on fetal and child development: A critical literature review. *Neurosci Biobehav Rev*, 43, 137-162.
- Gunnar, M.R. (1998). Quality of early care and buffering of neuroendocrine stress reactions: potential effects on the developing human brain. *Prev Med*, 27(2), 208-211.

- Hack, M., Wilson-Costello, D., Friedman, H., Taylor, G.H., Schluchter, M., & Fanaroff, A.A. (2000). Neurodevelopment and predictors of outcomes of children with birth weights of less than 1000 g. *Arch Pediatr Adolesc Med*, 154, 725-731.
- Hindmarsh, G.J., O'Callaghan, M.J., Mohay, H.A., & Rogers, Y.M. (2000). Gender differences in cognitive abilities at 2 years in ELBW infants. *Early Hum Dev*, 60, 115-122.
- Hoekstra, R.E., Ferrara, B., Couser, R.J., Payne, N.R., & Connell, J.E. (2004). Survival and long-term neurodevelopmental outcome of extremely premature infants born at 2326 weeks' gestational age at a tertiary center. *Pediatrics*, 113, e1-6.
- Lawrence, J., Alcock, D., McGrath, P., Kay, J., MacMurray, S.B., & Dulberg, C. (1993). The development of a tool to assess neonatal pain. *Neonatal Network*, 12(6), 59-66.
- Monique, A.A., Caljouw-Marguerite, A.C., Kloos-Madeleine, Y., Olivier-Ida, W., Heemskerk-Winke, C.R., & Pison-Gerben, D., et al. (2007). Verhoef measurement of pain in premature infants with a gestational age between 28 to 37 weeks: Validation of the adapted COMFORT Scale. *J Neonatal Nurs*, 13, 13-18.
- Msall, M.E., Buck, G.M., Rogers, B.T., Duffy, L.C., Mallen, S.R., & Catanzaro, N.L. (1993). Predictors of mortality, morbidity, and disability in a cohort of infants < or = 28 weeks' gestation. *Clin Pediatr*, 32, 521-527.
- Nelson, K.B. & Ellenberg, J.H. (1981). Apgar scores as predictors of chronic neurologic disability. *Pediatrics*, 68, 36-44.
- Noble, Y. & Boyd, R. (2012). Neonatal assessments for the preterm infant up to 4 months corrected age: a systematic review. *Dev Med Child Neurol*, 54(2), 129-139.
- Schneider, M.L. (1992). Delayed object permanence development in prenatally stressed rhesus monkey infants (*Macaca mulatta*). *Occup Ther J Res*, 12, 96-110.
- Schneider, M.L. & Coe, C.L. (1993). Repeated social stress during pregnancy impairs neuromotor development of the primate infant. *J Dev Behav Pediatr*, 14(2), 81-87.
- Score, A. (1986). Use and abuse of the Apgar score. *Pediatrics*, 78(6), 1148.
- The Apgar Score (2015). Committee Opinion No 644. American College of Obstetricians and Gynecologists. *Obstet and Gynecol*, 126(4), 52-55.
- Van den Bergh, B.R., Mulder, E.J., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neurosci Biobehav Rev*, 29, 237-258.
- Vohr, B.R., Wright, L.L., Dusick, A.M., Mele, L., Verter, J., & Steichen, J.J., et al. (2004). Neurodevelopmental and functional outcomes of extremely low birth weight infants in the National Institute of Child Health and Human Developmental Neonatal Research Network, 1993-1994. *Pediatrics*, 105, 1216-1226.
- Wood, N.S., Costeloe, K., Gibson, A.T., Hennessy, E.M., Marlow, N., & Wilkinson, A.R. (2005). The EPICure study: associations and antecedents of neurological and developmental disability at 30 months of age following extremely preterm birth. *Arch Dis Child Fetal Neonatal Ed*, 90, F134-140.
- Wood, N.S., Marlow, N., Costeloe, K., Gibson, A.T., & Wilkinson, A.R. (2000). Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. *N Eng J Med*, 343, 378-384.
- Woodward, L.J., Anderson, P.J., Austin, N.C., Howard, K., & Inder, T.E. (2006). Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. *N Engl J Med*, 355(7), 685-694.