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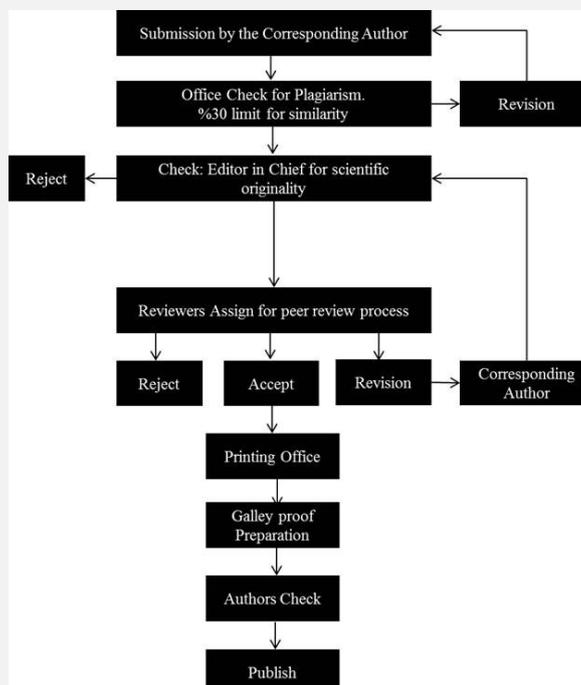
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Major acute pain complications in Congolese children with sickle cell disease

Lydie Ocini Ngolet^{1*}, Moyen Engoba², Alexis Elira Dokekias¹, Kocko Innocent¹, George Moyen²

Abstract

Objective: Sickle cell disease is the most frequent genetic blood disorder in the world and pain complications are the most prominent clinical aspects in sickle cell population. This study aims to describe the morbidity feature of major acute pain complications in children with sickle cell disease and outcome.

Material and Methods: 166 sickle cell disease children (4.3%) with a mean age of 85.31 months old \pm 60.40 admitted in the pediatric intensive care unit for major acute pain complications were enrolled in the study from January to December 2014. Major acute pain complications were defined as acute sickle cell related pain with an intensity assessed at 3 on the Wong-Baker faces pain rating scale.

Results: Over the period study, 118 patients were admitted for diffuse vaso occlusive crisis (70.09%). Localized vaso occlusive crisis occurred in 13.25%, acute chest syndrome in 09.64% and hand foot syndrome in 06.02%. The most common trigger factors were bacterial infections (65.12%) followed by malaria (34.88%). Mortality of 12.05% was recorded while 27.71% were discharged and 60.24% transferred to other departments. The mortality rate was significantly higher in the range age over 5 years ($p=0.004$)

Key words: Sickle cell disease, Major acute pain, Pediatric Intensive care department, Congo.

Introduction

Sickle cell disease (SCD) is the most prevalent blood disorder in the world. The highest prevalence occurs in Sub-Saharan Africa where 75% of 300,000 annual births are born in Africa (1). By the year 2015, there will be 50% increased in the number of affected births (2). SCD is a real public health issue in the Sub-Saharan region that contributes to major the rate of mortality among children whose data varies according studies (3,4). Acute pain complications are major symptoms of SCD and principal of cause hospitalization of children with sickle cell disease. In Africa they account in the pediatric intensive department for 1.8 to 6% (5, 6).

SCD has a prevalence of 0.9% in the Congo Brazzaville and is also a public health issue. The department of public health in the Congo has introduced diverse interventions such as free consultations for children in pediatric outpatient department at Teaching hospital and Sickle Cell Center. However, mortality remains high and the pattern of major acute pain complications in the PICD is unknown in the Congo. This current study describes the pattern of major acute pain complications in SCD children and their outcome in

the pediatric intensive care in the Teaching Hospital of Brazzaville in the Congo

Material and Methods

The study was conducted from January to December 2014 in the department of pediatric intensive care in the Teaching Hospital at Brazzaville.

Brazzaville is the biggest city of the Congo located in the south part of the Republic of Congo with a population of 4 millions. The Teaching Hospital is the biggest medical facility of the country where attend to almost all SCD patients living in Brazzaville. There is in Brazzaville only one pediatric intensive care department (PICD) that receives and manages all life threatening medical emergencies of children aged 1 month to 17 years old.

All medical records of children admitted during our study in the PICD were reviewed. Medical records with diagnosis of major acute pain complications were enrolled in the study. The diagnosis of SCD disease has been confirmed by hemoglobin electrophoresis on children that were identified initially from previous medical records.



Definition

Acute pain sickle cell episodes related are pain symptoms linked to the presence of abnormal hemoglobin (HbS). They can occur spontaneously or precipitated by infection, stress or dehydration.

Acute pain episodes are defined as major when, the intensity is assessed at 3 on the Wong-Baker faces pain rating scale. Acute pain episodes can be limited or diffuses when they affect multiple sites [9, 10].

The diagnosis of infection was based by the following clinical findings: fever over 38.5C or hypothermia<36.5C, tachypnea> 40 breaths per minute, “toxic-looking” associated with symptoms specifics to the infection developed.

Bacterial infections were: pneumonia, meningitis, angiocholitis, Acute Pyelonephritis and sepsis. Parasitical infectious were malaria. Pneumonia was defined as the presence of abnormal breath sounds and pathological chest X-ray. Meningitis was defined as stiff neck and abnormal cerebral spinal fluid. Angiocholitis was diagnosed when patient was presenting jaundice, pain in the right upper quadrant and mild hepatomegaly. Acute Pyelonephritis was associated flank pain, nausea, vomiting with positive urinary strip and urine culture. Hence, sepsis was defined by tachycardia, polypnea leukocytosis or leucopenia, and positive C-reactive protein. Report of blood culture are usually not released within a week, therefore are not available when in the patients are in the PICD, that is why distribution of microorganimes are not provided in the present study.

Aches and positive smear were defining malaria

Data abstracted from records were variables related to children: gender, age, length of time between beginning of symptoms and hospitalization, pre hospital consultation, length of hospitalization, diagnosis and outcome.

Patients

During the study period, 3,620 children were admitted in the PICD. Among them 188 (5.6%) children were diagnosed for acute SCD complications. Among the 188 children, 166 (4.2) were hospitalized for major acute pain episodes. Major acute pain complications was the first cause of hospitalization (88.30%) followed by hyperhemolytic crisis.

Statistical analysis

Data were entered into Microsoft Excel and analyzed SPSS (Chicago-USA). Categorical variable were described as proportion (percentage), continuous variables were described as medians (inter-quartile range) Differences between proportions were calculated using Fisher’s exact test The P-values or less than 0.05 were considered to be statistically significant.

Results

One hundred sixty six were enrolled in the study. They were 86 boys (51.81%) and 80 girls (48.19%) with a sex ratio of 1.07. Children were aged between 24 and 192 months old (mean age 85.31 ±6.40 months old). Almost two-third (72.89%) were below 5 years of age. In this study 94 children (56.63.7%) were coming from their homes, whereas 48 children (28.92%) were referred by primary and secondary medical facilities.

The time interval between the beginnings of the symptoms and the admission to the PICD ranged from 2 to 12 days (mean 3±1.1 days), whereas the duration of hospital admissions in PICD ranged from 1 to 16 days (mean 3±1.5).Table 1.

Table 1: Characteristics of 166 children with SCD admitted in PICD for major acute pain complications

Characteristics	
Gender n (%)	
Female	92 (48,9)
Male	96(51,1)
Sex ratio	1.04
Age (month)	
Mean ±SD	69.26±50.4
Min-Max	6-192
Range of age (months) n (%)	
1-24	57(30.32%)
25-60	64(34.04)
61-120	41(21.81)
>120	26(13.83)
Duration of illness (days)	
Mean ± SD	3±1.5
Min-Max	2-12
Coming from n(%)	
Teaching hospital departments	24(12,8)
Secondary health facilities	28(14,9)
Primary health facilities	20(10,6)
Home	116(61,7)
Lifetime hospitalization (days) n%	
1-2	88(46,8)
3-8	68(36,2)
9-16	32(17)

Table 2 summarizes the distribution of major acute pain syndrome. Diffuse vaso occlusive was the most common major acute pain episode observed in 71.09% patients followed by limited vaso occlusive (13,25%) and acute chest syndrome (09.64%).

Major acute pain syndrome were associated with infectious factors in 90.96% (n=151), without factors noticed in 09.04% (n= 15). Infections were due to bacterial infections (65, 12%) and malaria (34.88%).

Among those bacterial infections, pneumonia was observed in 61 patients (67.78%), pyelonephritis in 12 (13.34%), meningitis in 8 (08.89%), septicemia in 5 (05.56%) and angiocholitis in 4 (04.44%).

Table 2: SCD Severe acute complications and trigger factors

Sever acute complications	N	%
Severe acute hyperhemolysis crisis	88	46.81
Severe mixte crisis	52	27.66
Severe vaso occlusive crisis	36	19.15
ACS	4	11.11
Stroke	12	6,38
Total	188	

Table 3 shows that 46 (27.71%) patients were discharged, while 100 patients (60.24%) were transferred to other departments and 20 (12.05%) died. A comparison of outcome by range of age showed statistically relationship. Mortality rate was the highest when the children were older than 120 months (p=0.04).

Table 3. Outcome of the 188 children admitted in the PICD for SCD severe acute complications. *P=0.004

Outcome N(%)	
Discharged	46 (24.47)
transferred	110 (58.51)
death	32(17.02)
Age when died* (months)	
1-24	2(12,5)
25-60	0(00)
61-120	12(37.5)
>120	16(50)

Discussion

Demographics range of non major acute pain syndrome SCD related is fully identified in Brazzaville since it has been the subject of several publications (11-13). However, pattern of major acute pain complications SCD related have received little attention even though they have been reported to increase the mortality of children with SCD (11,13,14). The present study is the first in the Congo to attempt to report the feature major acute pain complications SCD related in children admitted in the PICD, and their outcome.

There is only one PICD in the Brazzaville region, which is the biggest city of the country. That explains the high proportion of children (28.92%) referred by primary and secondary health institutions. Our results should be interpreted bearing in mind the study setting. Indeed, data were collected in the PICD that admits only children aged 1 month to 17 years old, therefore had an inbuilt bias toward children aged 18 years. However, as we said previously, the PICD is unique; this study probably included all the majority of SCD children living in Brazzaville and then gives a

good picture distribution of SCD severe acute complications in Brazzaville.

One hundred eighty eight children (5.6 %) were admitted to the PICD for complications of sickle cell disease which is remarkable lower than Abhulimhen’s report but higher than Anyanwu’s findings (5, 15).

Our population study is young with a median age of 85.31 months (7 years). Among them, nearly two third of the population study were aged under 60 months (5 years). Similar age distribution has been described by different authors (5, 15-17). The first cause of admission in PICD with similar mean age is major acute pain complication (5, 15-17).

Feature of SCD’s complications vary according SCD children range of age (15). The authors agree on the predominance of hyperhemolytic crisis before the age of 5 vaso occlusive crises after the age of 5 (11-13). Nutritional deficiencies, acute chronic sequestration more frequent before the age of 5 to which is added malaria high infestation degree in Sub-Saharan Africa region are many aggravation factors of acute hyperhemolytic crisis that justify the clinical pattern distribution (14).

Non implementation of penicillin prophylaxis, pneumococcal and typhoid fever vaccines lead Infections to be first factors associated with sickle cell morbidity in children (10-18). Despite the fact that lake of effective laboratory facilities restricted the accurate diagnosis of bacterial acute febrile illness, distribution of the type of severe infection, in this current study was found to be similar to those described elsewhere (11,13,19-21). Pneumonia has been recognized as the main severe infection among sickle cell disease children. In fact, this clinical finding is not specific to the sickle cell disease population, since respiratory infections at the national level are the second cause of hospitalization in health facilities in the Congo (22).

Bacterial infections share similar findings between PICD and conventional pediatric departments in children with SCD. Meningitis accounted 08.89% in our study, 7.3% in Senegal and 6% in Nigeria (5,18). Septicemia rated 05.56% in our study and 4.1% in France (23). The prevalence of pyelonephritis (13.34%) was barely higher to the one reported in Brazzaville in conventional pediatric department, 10% à Brazzaville (11). However, osteomyelitis rate was higher than conventional pediatric departments (12,14,17).

Malaria is after bacterial infections the most common trigger acute sickle cell crisis in our region and second cause of hospitalization in sickle cell and not sickle cell pediatric population (5,6). Both population sickle cell and not sickle cell share comparable rate, even though we reported higher rate in our study (23). However, cerebral malaria is exceptional in the sickle cell population (21, 23,24).

ACS is an acute non infectious pulmonary complication seen in patients with sickle cell disease. It is one of the major causes of morbidity and mortality among children (25, 26). ACS's symptoms overlap with those of pneumonia and then can be sometimes very difficult to diagnose. That explains the quite diverse distribution reported (8,11,13,18).

Only one fourth of the patients (27.71%) were discharged while 20 (12.05%) were death. The outcome shows more severe outcome of the disease if we compare with Nigeria's findings (5,6,15,17).

Sickle cell disease in the western part of Africa, where the Nigeria is located, is known to have less severe morbidity and better outcome. Indeed, phenotypic modulator factors such high HbF levels, co-inheritance of α thalassemia and predominance of Senegal and Benin haplotypes are factors that may explain this difference (27).

The highest incidence of death is usually reported the in the first 5 years of life because children are at increased risk of life threatening infections due to absent or non functional spleens and a decreased immune response (28).

Paradoxically, in our study the lowest mortality rate is shown in that rate of age. That particularity also raised by Diagne and al deserves to be confirmed substantiated more thorough prospective study (18).

Conclusion

Major acute pain complications are predominantly marked by diffuse vaso occlusive crisis and triggered by infections. This enhances the relevance of early intervention as neonatal screening, penicillin prophylaxis, immunization but also malaria prophylaxis

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was completed due to defined rules by the Local Ethics Commission guidelines and audits.

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Prediction by maternal risk factors and prenatal care of neonatal intensive care of neonatal intensive care admission in a University Hospital, Turkey, a case control study

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Abstract

Objective: To determine socioeconomic characteristics, prenatal care and maternal risk factors and reveal the impact on newborn, in mothers who gave birth .

Material and Method: A case-control study comparing the mothers whose babies were admitted and mothers whose babies were not admitted to neonatal intensive care unit of a University Hospital. The 200 women as a case and 200 women as a control has been chosen among total 958 female patient. A survey form has been filled by the patient to determine socio-economic and prenatal care features and the risk factors. The APNCU index is was used for adequacy of prenatal care. Chi square test, Fisher's exact test and multiple logistic regression analysis are were used for statistical evaluation.

Results: As to prenatal care 94.3 % of the mothers received adequate amount and 95.2 % adequate content. The location of residence (OR:2.72), husband education (OR:1.97), spontaneous abortion in second trimester or preterm birth history (OR:4.27), multiple pregnancy (OR:5.25), bigger or smaller uterine size (OR:26.58), early uterine contraction (OR:2.21), and problems during delivery (OR:2.53) variables were related to be in neonatal intensive care unit.

Conclusion: Factors related to being in intensive care found in this study should be understood and interpreted in all of the steps of health services, and interventions should be executed when necessary.

Keywords: Prenatal care, maternal risks, neonatal intensive care.

Introduction

In clearing up the problems of the high risk newborn to be considered due to the anatomic and physiological differences from the healthy newborn, methods containing special tools and care are required to be used and watched in neonatal intensive care unit (NICU) [1].

Several risks related to the mother are known to increase the risk of babies to be in intensive care [2]. A qualified prenatal care (PNC) service primarily provides to determine and harness the risks endangering pre-pregnancy and during pregnancy in the future mother and therefore provides the prevention of negative results which can occur both in the mother and the newborn [3,4].

Studies done presents that inadequate PNC is related to preterm labor, low birth weight an newborn deaths [5,6].

Besides PNC, interventions during birth and right after that are important and deliveries should be made by health personnel and NICU's should be at least found in certain centers.

It is important to determine the factors affecting the intense care requirement of the newborn in terms of creating effective interventions to be made in this respect in the whole process starting from prenatal period.

This study aims to compare the mothers delivering between January – June 2010 in Hacettepe University Obstetrics and Gynaecology Clinic whose babies were admitted and whose babies were not admitted to NICU and determine the effects of socio-economic factors, prenatal care received risk factors during pregnancy and delivery on the new-born's being in intensive care.

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Material and Methods

This study is an analytic one with case/control type comparing the mothers whose babies were admitted and whose babies were not admitted to NICU and researching the factors effective on the admission to NICU. The study is conducted on women who gave birth in Hacettepe University Hospital Gynaecology Clinic between January–June 2010. Because of being a third step hospital, this hospital is the one appealed more by risky pregnancies. In general, the babies born under 2500 gram or before completing the 37th pregnancy week and/or in need of special care are monitored at NICU. In this period 200 women whose babies admitted to NICU were taken as a case group and 200 women whose babies not admitted to NICU were selected by simple random sampling method among total 958 women as a control group.

In total 253 infants of the 210 women in this six-month period were in intensive care. 200 women and 239 babies (33 twins and 3 triplets) of them were enrolled in the study. 200 women and 207 babies (seven twins) were selected from the remaining 748 women by the method of random sampling as the control group. In this way, the study was carried out on 400 mothers, 400 births and 446 newborns. While the dependent variable of the research was babies' hospitalization at NICU, many variables related to the socioeconomic level, PNC status of the mother and risk factors in pregnancy were independent variables.

In the collection of the data, primarily the mothers were informed about the research and after taking written consents, a survey form containing questions determining socioeconomic and PNC features as well as the risk factors form prepared by using the list found in Turkish Ministry of Health program was filled in by face-to-face method [7, 8]. Furthermore, delivery records and NICU records were used for the information related to the present statuses of both mothers and newborns.

In PNC evaluation, information such as PNC number of monitoring, on which month it started, by whom and what was done was taken. According to Adequacy of Prenatal Care Utilization (APNCU) index which presents a PNC number by taking the week when PNC started and the week delivery happened into consideration; it was evaluated as "inadequate", "intermediate", "adequate" and "adequate plus" [9]. Furthermore, failure to perform any one of weight measurement, blood pressure measurement, and urine and blood examination, ultrasound examination was evaluated as inadequate PNC in qualitative terms.

The data were analysed by entering in Statistical Package for Social Sciences (SPSS) 15.0 program. In order to determine the factors affecting the condition of admission to NICU,

Chi square test, Fischer's exact test, student's t-test and as a multivariate analysis, multiple logistic regression analysis was used in statistical evaluations.

Results

When the conditions of those at the intensive care were evaluated, it was clear that 139 infants (58.2%) were below 2500 gram (more than half of them under 2000gram) and 84 infants (42 %) were being born under 37 weeks. In contrast, 10 infants from the control group (4.8%) are between 2000 to 2500 g, and 14 infants (7%) are born under 37 weeks. It shows that there is one or more diagnoses that may require intensive care in all the files of the infants at the intensive care. The diagnoses such as miscarriage or premature, IUGR, SGA might be accepted as the greatest diagnosis group with 66.5% in total. Besides, it showed that the diagnoses such as respiratory distress (20%), MSS, KVS, GIS, UGS anomalies (20%) congenital heart disease (6%), blood disorders (3.5%) create significant rates and some other diagnoses were in small numbers.

Some socio-economic features of the babies of mothers participating in the research according to the condition of being in NICU is seen in Table I. When age is considered, 25-35 years old groups form the highest rate in whole group (63 %). There are total 4 women under 18 years old and their babies were in NICU. Mothers over 35 years old, on the other hand, show a higher rate in the group whose babies were in NICU but differences were not found to be statistically significant ($p=0,097$).

When compared in terms of residing places, it was seen that those who were not in NICU more substantially resided in Ankara city centre. Those residing in a district, village or other cities, on the other hand, are in higher rate in the case group when compared to the other group ($p=0,000$). No statistically significant difference was found between the groups in terms of women's educational backgrounds and occupations ($p=0,818$) ($p=0,115$). When we look at the educational backgrounds of the spouses of the mothers, primary school graduation of the fathers in case group and high school graduation of the fathers in control group is significantly high ($p=0,003$).

No statistically significant relationship was found between the occupations of the fathers and babies' being in NICU ($p=0,121$). No significant difference was found between the groups when the annual income per person was compared ($p=0,749$).

Table 1. Distribution of some socio-economic features of the mothers participating in the research according to the condition of their babies' being in NICU

Condition of being in intensive care unit			
Socio-economic Factors	Cases	Controls	Statistic (X ² and p)
	n=200 %	n=200 %	
Age of the mother			
18 and younger	2,0	0,0	X ² =6,330 p=0,097
19-24	18,0	24,0	
25-35	63,5	62,5	
Above 35	16,5	13,5	
Residing place			
Ankara centre	63,0	84,0	X ² =22,642 p=0,000
Districts-Villages and Other cities	37,0	16,0	
Educational background			
Primary school	35,5	32,5	X ² =0,401 p=0,818
High school	31,5	33,0	
University	33,0	34,5	
Occupation of the mother			
Housewife	67,0	58,0	X ² =5,922 p=0,115
Self-employed	8,5	15,5	
Officer	23,0	24,0	
Worker	1,5	2,5	
Educational background of the spouse			
Primary school	29,0	16,5	X ² =11,430 p=0,003
High school	28,0	40,5	
University	43,0	43,0	
Occupation of the spouse			
Unemployed	2,0	0,0	X ² =5,812 p=0,121
Self-employed	53,0	60,0	
Officer	32,5	30,5	
Worker	12,5	9,5	
Annual income per person (TL)			
≤ 5000	37,5	34,5	X ² =0,577 p=0,749
5000-9999	26,0	29,0	
≥ 10000	36,5	36,5	

Table 2: Distribution of PNC of the mothers which was evaluated with APNCU index, according to the condition of babies' being in NICU

Condition of being in intensive care unit				
Prenatal care with APNCU	Cases	Controls	Total	Statistic (X ² and p)
	n=200 %	n=200 %	n=400 %	
Inadequate	2,5	0,5	1,5	X ² =17,629 p=0,001
Intermediate	2,0	6,5	4,3	
Adequate	13,5	25,5	19,5	
Adequate plus	82,0	67,5	74,8	

The mean number of prenatal visit was 14.04 ± 5.90 in case group, and 14.42 ± 4.68 in control group and there is no significant difference between the groups ($p=0,219$) and the whole group was seen to be substantially monitored by a specialist physician. Mean number of antenatal visit by a specialist physician is 13.14 ± 5.83 in the case group, and 13.90 ± 4.24 in control group. There were only 3 women who received antenatal care less than 4, in whole group. Results obtained according to APNCU index for PNC has been given in Table II.

Accordingly it is seen that 'adequate plus' PNC is received in the large part of the group. While 'Inadequate' and 'Adequate Plus' monitoring is higher in case group, 'Intermediate' or 'Adequate' monitoring is higher in control group when compared to the other group ($p=0,001$). When PNC content is evaluated in 3 persons weight, in 3 persons blood pressure, in 3 persons blood count, in 14 persons urine and in 1 person USG examinations were not performed in the whole group and total 19 persons to whom one of these tests were not applied. In this sense, qualitatively inadequate PNC ratio is 5, 5 % in case group and 4 % in control group ($p=0,481$).

Those which are determined to be statistically significant in bivariate analysis in the distribution among the risks determined in the histories and present pregnancies of mothers participating in the research according the condition of their babies' being in NICU are shown in Table III. When personal risk factors of the mothers are evaluated, having received infertility treatment was found in a higher ratio in intensive care group ($p=0,002$). Number of deliveries being 5 or greater ($p=0,000$) in relation to their previous obstetrical histories, stillbirth or neonatal death ($p=0,005$), spontaneous abortion in 2nd trimester or preterm labor ($p=0,000$) was found statistically significantly high in those who are in NICU.

When present pregnancies of mothers are evaluated, changes in fetal movements, gestational hypertension, multiple pregnancy, polyhydramnios or oligohydramnios, small/big uterus according to week, early membrane rupture, early contractions, urinary infection and preeclampsia was found significantly high in mothers whose babies are in intensive care when compared to the other group. Important fetal problem (IUGR, SGA, congenital heart disease, congenital anomalies etc) suspected by USG during pregnancy was found to be significantly high in those whose babies are in NICU ($p=0,000$).

Having a problem during delivery was found to be higher in mothers whose babies were in NICU ($p=0,003$).

Among the factors not given in the table but researched about previous pregnancies, no statistically significant difference was found between frequent delivery, small or big babies according to the gestational age, baby with a fetal malformation, habitual 1st trimester abortion, gestational hypertension, placenta retention or postnatal bleeding, Rh isoimmunisation or hydrops fetalis and intervened delivery and to be in intensive care.

Likewise, among the risks researched in relation to their existing pregnancies, anaemia, excessive/low weight gain, shortness of height, hyperemesis gravidarum, vaginal bleeding cervical failure, presentation disorder, fetal head's inability to settle in primigravid in the 40th week, existence of gestational diabetes, genital infection and chronic disease was not found related to being in NICU.

Multivariate Analysis (Logistic Regression Analysis) Results:

With bivariate analyses risks, which are considered important, do not much include each other and are numerically adequate were examined with logistic regression analyses.

Accordingly, residing place, educational background of the spouse, infertility treatment, number of deliveries ≥ 5 , stillbirth in the previous delivery or neonatal death, spontaneous abortion in 2nd trimester or preterm labor in the previous pregnancy, gestational hypertension, multiple pregnancy, polyhydramnios or oligohydramnios, small/big uterus according to week, early contractions, urinary infection, preeclampsia and problem during birth variables were taken to logistic regression analysis and results related to the factors which are found effective are shown in Table IV.

Accordingly, babies' risk of being in intensive care increased 2,72 times in those living in a city other than Ankara, another district or village, 1,97 times in those whose spouse's educational background is primary school graduation when compared to those whose spouse's educational background is university graduation, 4,27 times in those who had spontaneous abortion in 2nd trimester or preterm labor in the previous pregnancies, 5,25 times in those with multiple pregnancy.

26,58 times risk increase was seen in those with small or big uterus according to pregnancy week, 2,21 times risk increase in those with early contraction, 2,53 times risk increase in those with problems during delivery.

Table 3: Distribution of the risks determined in the histories and present pregnancies of the mothers according to the condition of babies' being in NICU (Those which are statistically significant)

Condition of being in intensive care unit			
Risks in the histories	Cases	Controls	Statistic (X^2 and p)
	n=200%	n=200	
Infertility treatment			
Yes	20,0	9,0	$X^2=9,760$ p=0,002
No	80,0	91,0	
Number of deliveries ≥ 5			
Yes	6,5	0,0	$X^2=13,437$ p=0,000
No	93,5	100,0	
Stillbirth or neonatal death			
Yes	16,0	7,0	$X^2=7,959$ p=0,005
No	84,0	93,0	
Spontaneous 2nd trimester abort/preterm labor			
Yes	18,0	5,0	$X^2=16,605$ p=0,000
No	82,0	95,0	
Risks in the present pregnancies			
Changes in fetal movements			
Yes	4,5	0,5	p=0,020*
No	95,5	99,5	
Gestational hypertension			
Yes	12,5	5,0	$X^2=7,045$ p=0,008
No	87,5	95,0	
Multiple pregnancy			
Yes	18,0	3,5	$X^2=21,914$ p=0,000
No	82,0	96,5	
Polyhydramnios or oligohydramnios			
Yes	18,0	11,0	$X^2=3,952$ p=0,047
No	82,0	89,0	
Small/big uterus according to the gestational week			
Yes	16,0	1,0	$X^2=28,930$ p=0,000
No	84,0	99,0	
Early membrane rupture			
Yes	14,5	2,0	$X^2=20,642$ p=0,000
No	85,5	98,0	
Early contractions			
Yes	35,5	15,5	$X^2=21,055$ p=0,000
No	64,5	84,5	
Urinary infection			
Yes	29,5	19,5	$X^2=5,406$ p=0,020
No	70,5	80,5	
Preeclampsia			
Yes	9,0	1,5	$X^2=11,308$ p=0,001
No	91,0	98,5	
Problems of the baby during pregnancy**			
Yes	34,5	4,0	$X^2=59,845$ p=0,000
No	65,5	96,0	
Problem during birth***			
Yes	18,0	8,0	$X^2=8,842$ p=0,003
No	82,0	92,0	
*: Fischer's exact test			
**: Small for gestational age, intra-uterine growth retardation, congenital anomalies etc.			
***: Early membrane rupture, cord entanglement, cord prolapse, pres			

Table 4. Results related to the factors which are found to be effective to be in NICU in logistic regression analysis

Risk Factors	Beta	Standard Error	p	Odds Ratio (OR)	95% Confidence Interval for OR	
					Lower Limit	Upper Limit
Residing Place Ankara-Centre Other Cities/district-village	1,003	0,275	0,000	2,726	1,591	4,668
Education of the spouse University Primary school High school	0,681 0,251	0,301 0,273	0,011 0,024 0,357	1,976 0,778	1,094 0,455	3,567 1,328
Spontaneous abortion in 2nd trimester or preterm birth history No Yes	1,453	0,404	0,000	4,276	1,936	9,445
Pregnancy status Single Multiple	1,659	0,464	0,000	5,255	2,117	13,043
Uterus according to the week Normal Small/big uterus	3,280	0,759	0,000	26,583	6,003	117,710
Early contractions No Yes	0,796	0,285	0,005	2,218	1,268	3,880
Problems during birth No Yes	0,930	0,360	0,010	2,534	1,252	5,128

Discussion

When the relationship between the socio-economic features and babies' being in NICU is evaluated (Table I), it is remarkable that there are total 4 mothers under 18 years old which is the risky age group in the age distribution of mothers and their babies are all in intensive care. Women older than 35 years old were more in number in this group but no statistically significant differences were seen between the groups in terms of age distribution.

This condition can be originating from the study group's not being numerically so high. Adolescent pregnancies and advanced age pregnancies are known to have results such as miscarriage/stillbirth or risky neonatal [10].

When the residing places of the mothers are evaluated, it was seen that those whose babies were in NICU resided in a place other than Ankara city centre in a higher rate when compared to the other group ($p=0,000$). This difference was found significant in logistic regression analysis as well (OR:2,72).

This can demonstrate the fact that socioeconomic factors are effective on being in intensive care. However, referral of risky considered patients living in the regions other than Ankara to the University Hospital in which the study was made can also be effective on this result.

No statistically significant difference was found between the groups in terms of educational backgrounds of the mothers ($p=0,818$). When compared to Turkey Demographic and Health Survey 2008 (TDHS-2008) data, educational backgrounds of women in the research group were seen to be better than Turkey-wide [10]. When the occupations of mothers were evaluated, it was seen that they were largely housewives and no significant difference was seen between the groups in terms of occupations ($p=0,115$). As in Turkey-wide, the ratio of working women in the research group is also not in adequate level [10].

The relationships between the educational backgrounds of the spouses of mothers and being in intensive care are statistically significant ($p=0,003$).

The educational level of fathers is higher in control group. This was determined as an important factor at the end of multiple analyses, too (OR: 1,97). Factors related to the father were found effective in similar studies in Turkey [11]. In our study group, fathers' educational level was higher when compared to mothers and it can be said that it has an effect on the social status and health results of the family. No statistically significant relationship was found between the occupations of fathers and babies' being in NICU. However, it is meaningful that there are total 4 unemployed fathers and their babies are all in intensive care. There is no significant difference in terms of income between the groups ($p=0,749$). On this result, economic levels of the patients making application to this hospital being close to each other and difficulties in taking income information can be effective.

The mean number of prenatal visits in the research group was close to each other and is about 14 and quite high in each group. This result is affected by the fact that our research was executed in an urban region and on those who gave birth in the University Hospital. WHO have suggested four monitoring based routine approaches for the large part of women as the new model of PNC and additional controls to those with special risks. This approach was introduced and used in several countries [12,13]. However, new 4 control PNC approach is not adequate in high risk pregnancies and multiple pregnancies. Number of prenatal visits is quite high in our study and less than 4 was seen only in 3 persons within the group.

PNC is generally known to be related to preterm labor, low birth weight, fetal death and neonatal death [5,6,14,15]. However, number of PNC evaluated in several studies is different from each other and numbers greater than 4 can be suggested according to results [15]. The process during PNC visits and status of the pregnant woman allows giving more correct decision for this number.

In a study done on those giving birth in a University Hospital in Ankara in 1996, average number of PNC are found as 8,7 and this is a lower average according to our study [16]. This shows that the number of PNC in Turkey, at least in urban region increased in time. However, although a large number of control ratios are required in complicated pregnancies, it also makes one think about whether the sources are effectively used in other circumstances.

When quantitative adequateness of PNC is evaluated according to APNCU index, it is seen that a large part of the group received adequate plus PNC (Table II). The sum of those who received adequate and adequate plus PNC is 94, 3% in the whole group. This result was found lower in a study executed on-site in Turkey with the same index [11]. Almost all of those who received inadequate PNC (which are few) are in intensive care unit. Those who received "intermediate" and

"adequate" PNC is higher in the control group and "adequate plus" PNC is higher in the case group.

These differences between the groups are statistically significant ($p=0,001$). The results obtained in our study have shown that those monitored in "inadequate" level as well as risky pregnant women are determined and monitored more, and thus those who are monitored "adequate plus" are in the higher ratio in the group which is in NICU.

It was seen that pregnant women in the study group were substantially controlled by specialist physician. In TDHS 2008 data, it was seen that PNC was taken 90% from the physician, and specialist and practitioner ratios were not specified. The high rate of received PNC by the specialist physician in our study shows that primary care health services are not sufficiently used.

When PNC's content was evaluated, it was seen that the number of persons to whom "inadequate" monitoring was made in qualitative terms was very low and so significant difference could be found between the groups in this respect ($p=0,481$). This result is an expected condition in our study group whose number of visits is very high and it is higher than the performance rates of the examinations in TDHS 2008 data [4].

As seen in Table III, having received infertility treatment is higher in those who are in NICU when compared to the other group ($p=0,002$). As a result of the infertility treatment which is gradually widespread today, multiple pregnancy rates increase and in multiple pregnancies low birth weight and other problems increase intensive care requirement. Among the risks related to the previous birth histories of mothers; number of births being 5 or greater, stillbirth or neonatal death, spontaneous 2nd trimester abortion or preterm labor is higher in those whose babies are in NICU. Existence of spontaneous 2nd trimester abortion or preterm labor history is also one of the factors remaining effective as a result of logistic regression analysis (OR=4, 2) (See Table IV).

When the risks which are determined in the current pregnancies of mothers (Table III) are evaluated, changes in fetal movements, gestational hypertension, multiple pregnancy, polyhydramnios or oligohydramnios, small/big uterus according to the week, early membrane rupture, early contractions, urinary infection and preeclampsia was significantly high in mothers whose babies are in NICU. The possibility of staying in intensive care unit is higher for the babies whose mothers have such risky conditions in their pregnancies. These relationships were shown in several studies [2,17].

Multiple pregnancies which are found to be significant in logistic regression analysis as well (OR=5, 25) increased with the spread of infertility treatment and they are high risk pregnancies due to their fetal and

maternal complications. Multiple pregnancies which are the most important factor found to be related to intensive care in the USA constitute 14% of neonatal deaths and increase perinatal mortality 10 times [2,18].

Since the existence of big or small uterus according to the week, which is one of the risk factors found significant (OR=28,5) in logistic regression analysis, reflects fetal growth and conditions related to amnion liquid, it can be a good indication of NICU requirement of the baby. Early membrane rupture is one of the most important preterm labor reasons and one of the factors affecting the babies' being in NICU and it has also taken place within the title of problems during birth in our study. Early contraction is also a condition increasing preterm labor risk. This factor was evaluated with logistic regression analysis and found significant (OR=2, 2). Conditions such as urinary infection and preeclampsia are also the factors resulting in prematurity [19, 20].

While the existence of a fetal problem as a result of USG examinations made in pregnancy is 34, 5% in the cases and it is only 4% in the controls (p=0,000). This result also demonstrates the fact that giving birth in a hospital with NICU is of vital importance if there is a problem detected in the baby during pregnancy.

A statistically significant relationship was found between having a problem during delivery in those participating in the research and the babies' being in NICU (p=0,003). This factor was also found to be significant in logistic regression analysis, (OR=2, 5), (See Table IV). In the study, the majority of the ones under the title of problems during the delivery consisted of EMR, and there were also problems such as cord entanglement, cord prolapsed and presentation anomaly.

Problems such as cord entanglement, cord prolapse, early membran rupture, presentation anomaly makes delivery difficult and increases the intensive care requirements of the babies.

Conclusion

In conclusion, in our study, being in NICU was found to be related to some socio-economic factors. Although PNC ratio is generally high, the approach of bringing qualitative PNC service to all parts of the community maintains its importance. Since PNC was inadequate within primary health care services, its integration to the first step should be made, specialist support should be given when necessary. And PNC visits more than required in pregnant women should be reviewed in terms of effective use of sources. Risks determined in the previous pregnancies and during control of mothers are extremely important, factors related to being in intensive care found in our study should be understood and interpreted in all of the steps of health services, and

interventions should be executed when necessary. When a problem occurs during pregnancies, the intensive care requirement of the baby should be substantially foreseen, access should be provided to suitable delivery conditions and NICU.

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Ethical issues: All Authors declare that originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the authors responsibilities. The study was completed due to defined rules by the Local Ethics Commission guidelines and audits.

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Aneurysm of the Internal Carotid Artery Pressing on Dorello's Canal in a Patient with Bilateral Abducens Nerve Palsy: Case Report

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Abstract

Objective: Abducens nerve palsy (ANP) has an incidence of 11.3/100,000. ANP related to pressure on an aneurysm on Dorello's canal is unusual. We report a case of bilateral ANP following head trauma.

Case: A 31-year-old woman was admitted for evaluation of diplopia that began after a trauma. In the diagnostic imaging, the magnetic resonance imaging (MRI) revealed a normal course of the bilateral abducens nerve (AN) in the pontine cistern. The adjacent anatomy of the right AN from the pons to the ocular bulb was normal. But the distal part of the left ICA petrous segment at the level of the foramen lacerum had a remarkable loss of signal void. Multidetector computed tomography angiogram demonstrated a left distal petrous ICA aneurysm which was under Dorello's canal and was remodeling the clivus.

Conclusion: We estimated that the left ANP was caused by the pressure of the aneurysm. and the right ANP was probably due to the trauma the patient had experienced.

Keywords: Abducens Palsy, Aneurysm, Dorello's Canal, MRI, Trauma

Introduction

The abducens nerve (AN) enters Dorello's canal after passing through the pontine cistern. The canal is located between the meningeal and periosteal layers of the dura mater just below the posterior clinoidal process. Trauma is the most common reason for bilateral abducens nerve palsy (ANP).

The nerve is injured by the shearing effect of trauma within the canal, where the nerve is held tightly (1). The second most common cause of ANP is subarachnoid hemorrhage of aneurysms and arteriovenous malformations (2), and the third most common cause is brain tumor, either because of direct invasion or as an effect of increased intracranial pressure (2).

ANP caused by tumor invasion generally occurs at the brainstem, in the pontine cistern, or at the cavernous sinus (3-5).

Here, we report a case of bilateral isolated ANP caused by head trauma on the right side and an unruptured aneurysm of the petrous internal carotid artery at the foramen lacerum pressing on Dorello's canal on the left side.

Aneurysm of the internal carotid artery (ICA) located at the level of the skull base has rarely been mentioned in the literature (6), and we have not found any report specifically describing an aneurysm in the petrous portion of the ICA pressing on Dorello's canal.

Case Report

A 31-year-old woman presented with the complaint of binocular horizontal diplopia at distance fixation in the primary position after an incident of head trauma 1 week prior (Fig. 1). She stated she had hit her head to the kitchen marble while standing up. She had been seen by an ophthalmologist 2 months earlier, when she presented with a 1-month history of diplopia of both the right and left lateral gazes.

On ophthalmological examination, her vision was 20/20 with the Snellen Chart. Examination of the anterior segment and fundus revealed no abnormality. The patient's pupils were equal, round, and reactive to light without any afferent pupillary defect. A 12-prism diopter (PD) esotropia was measured at a distance, and there was a limitation of abduction in both eyes.

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She had no systemic diseases such as diabetes mellitus, hypertension, or collagen tissue disorders. To investigate the etiology of bilateral ANP, magnetic resonance imaging (MRI) including the constructive interference in steady state (CISS) sequence of the brainstem and pontine cistern was initially scheduled.

The CISS sequence images through the medulla and pons demonstrated a normal course of the bilateral ANs (Fig. 2) ascending from the pontomedullary junction to Dorello's canal.

The course of the right AN from the pons up to the lateral rectus muscle of the ocular bulb and the adjacent anatomy was normal. But in the axial images of the skull base, especially on T2WI, the distal part of the left ICA petrous segment at the level of the foramen lacerum had a remarkable loss of signal void (Fig.3). Multi-detector computed tomography (MDCT) angiography demonstrated a left distal petrous ICA aneurysm located under Dorello's canal that was remodeling the clivus (Fig. 4a, b).

The size of the aneurysm was $12.6 \times 9.3 \times 8.6$ mm. We conjectured that the left ANP was caused by the pressure of the aneurysm on Dorello's canal, and the right ANP was probably due to the trauma the patient had experienced.

Anticoagulation therapy was administered to the patient, and endovascular intervention of the aneurysm was planned for treatment of the left ANP. The patient was also administered systemic corticosteroid therapy for the traumatic ANP on the right side.

Two days after the placement of a carotid stent in the left ICA aneurysm (Fig. 5a, b), the patient's left eye was completely recovered from esotropia and the limitation of abduction. The palsy of the right abducens nerve improved within a month.



Figure 1. Eye movements of the patient demonstrating bilateral abducens palsy



Figure 2. The CISS sequence in axial plane shows the cisternal portion of the abducens nerves at the level of the origin of Dorello's canal (white arrows).

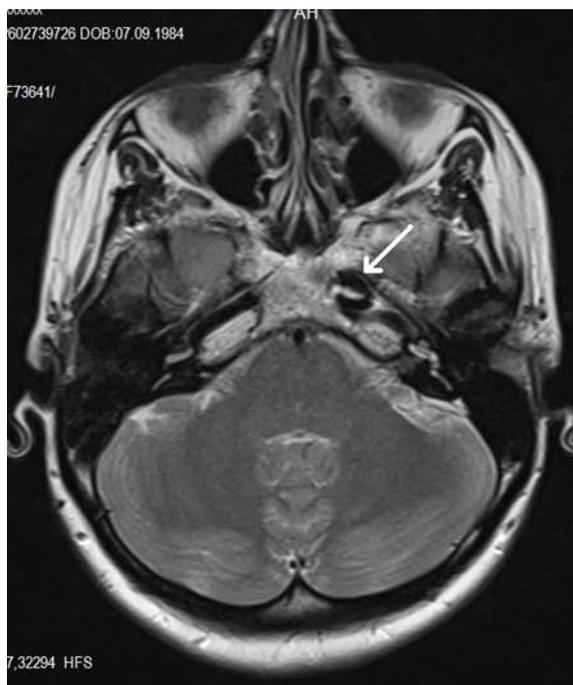


Figure 3. The axial image of T2-weighted sequence at the level close to the Dorello's canal. The distal part of the left ICA petrous segment had a remarkable loss of signal void in the central lumen (white arrow).

Discussion

The nucleus of the AN is located in the dorsal pons. Its course from the nucleus to its innervation of the lateral rectus muscle can be divided into four parts: the nucleus and intraparenchymal portion, cisternal portion, cavernous sinus portion, and orbital portion. The AN passes through the pontine cistern and enters the dura at the base of the skull, where it courses through Dorello's canal before entering the cavernous sinus (7). Dorello's canal has been defined as the small space located between the two dural leaves below the posterior clinoid process and the most anteromedial portion of the petrous ridge (8). The canal extends from the point where the AN pierces the dura mater to its entrance into the cavernous sinus. Its length is 4 to 13 mm (9). The petrosphenoidal ligament, or Gruber's ligament, is the posteromedial limit of the canal, connecting the petrous ridge to the clivus. The AN sheath has multiple connective tissue attachments to Gruber's ligament and the endosteal dura mater in Dorello's canal. These attachments limit the mobility of the nerve in compressive or stretch injuries, and the part of the nerve affected by trauma is generally this segment within the canal (1, 10). Avulsion injury may be the mechanism of ANP in the absence of evident fractures, as in the present case. While Dorello's canal cannot be directly revealed with radiological imaging techniques, the surrounding structures constituting the canal can be assessed. All 4 portions of the nerve should be radiologically normal for isolated posttraumatic ANP to be diagnosed.

In the literature, ANP related to an aneurysm is generally bilateral and results from bleeding of the aneurysm (11). Subarachnoid bleeding affects the cisternal portion of the AN. ANP can also be caused by a direct aneurysmal mass effect without bleeding on the AN, and this rare effect usually occurs at the cavernous sinus (12). ANP does not frequently occur because of pressure from an aneurysm on Dorello's canal; the left nerve palsy of our patient was due to the pressure of the distal petrous ICA aneurysm on the canal, as indicated by the patient's quick recovery from nerve palsy after stent treatment.

The main radiological approach to investigating ANP is MRI. But it is difficult to identify the AN clearly using conventional MRI sequencing due to its long course up to the cavernous sinus from the brainstem. Advanced MRI sequences have improved our ability to visualize the cisternal portion of the AN. In particular, T1-weighted 3D magnetization-prepared rapid gradient-echo (MP-RAGE) imaging and heavily T2*-weighted 3D CISS sequences with 1-mm section thickness on the axial and sagittal planes can provide detailed images of the cisternal portion of the AN (13).



Figure 4a/b. MDCT angiogram in axial and coronal plane image. There was a left petrous ICA aneurysm at the level of foramen lacerum which was close to the Dorello's canal and remodeling the clivus (black arrows)

To investigate neural parenchyma-induced etiologies, the fluid-attenuated inversion recovery (FLAIR) sequence should be performed to confirm suspicion of multiple sclerosis in young patients, and DWI should be performed for suspicion of ischemia in elderly patients (14, 15). In order to assess the level of the nerve between the cisternal and orbital portion, axial and coronal T1WI with contrast medium is needed to search for a possible brainstem tumor, infectious or malignant meningeal disease in the basal cisterns, cavernous sinus infectious disease, or a sellar mass (16).

As in our patient, the skull base should be carefully evaluated to investigate the etiology of ANP because of the possibility for an aneurysm or mass to be settled in this region. In the diagnosis of subarachnoid hemorrhage and hydrocephalus causing ANP after trauma or ruptured aneurysm, CT is the first imaging modality that should be performed. CT and MR angiography are minimally invasive imaging methods and should be the first choices for investigating an aneurysm on the circle of Willis.

Traumatic ANPs are usually observed immediately after a head trauma, and the rate of spontaneous recovery from ANP without underlying etiology is 84% in unilateral palsy and 38% in bilateral palsy 1. The main treatment of ANP is intended to the etiology.

Abducens nerve palsy related to pressure of an aneurysm on Dorello's canal has not yet been reported in the literature.

Accordingly, the skull base should be carefully evaluated to investigate the etiology of abducens palsy.



Figure 5a. Lateral angiogram obtained before treatment shows a left petrous ICA aneurysm.



Figure 5b. Posttreatment lateral view shows exclusion of the aneurysm and the reconstructed internal carotid artery.

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