процессов характеризуются тяжелым течением и неблагоприятным исходом. ДЗЛ является диагностической проблемой для профессиональных педиатров и пульмонологов. В каждом отдельном случае, с целью выбора правильной тактики лечения необходимо тщательное проведение дифференциальной диагностики с применением многосторонних методов обследования, исключение наиболее частых патологий, таких как инфекционные заболевания легких (пневмония, туберкулез), структурные аномалии дыхательных путей, иммунодефицитные состояния, врожденные аномалии сердца, муковицидоз.

რეზიუმე

ფილტვის ინტერსტიციული დაავადება - კლინიკური შემთხვევის დემონსტრირება

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შრომის მიზანს წარმოადგენდა ბავშვთა ასაკში ფილტვის ინტერსტიციული დაავადების ადრეულ სტადიაში გამოვლენა, მათი სწორი დიაგნოსტირება, მკურნალობის ტაქტიკის ჩამოყალიბება და შედეგად სიცოცხლის ხანგრძლივობის, ხარისხის გაუმჯობესება.

ფილტვის ინტერსტიციულ დაავადებათა ჯგუფში ერთიანდება 200-ზე მეტი მწვავე და ქრონიკული დაავადება ანთებითი და ფიბროპროლიფერაციული ცვლილებებით. მათი დიაგნოსტირება რთულია და ვერ ხერხდება რენტგენოლოგიური მონაცემების საფუძველზე. რთულია მათი გარჩევა ფილტვის ბაქტერიული დაავადებებისგან, განსაკუთრებით პნევმონიებისა და ტუბერკულოზისგან, რაც ხშირად განაპირობებს არასწორ მკურნალობას, დაავადების პროგრესირებას და სავალალო გამოსავალს.

სტატიაში წარმოდგენილია კლინიკური შემთხვევა, რომლის ანალიზი მოხდა ლიტერატურაში არსებული დიაგნოსტიკური და დაავადების მართვის კრიტერიუმების საფუძველზე. სტატიაში დეტალურად განხილულია სხვადასხვა კლინიკური კვლევების შედეგების საფუძველზე ჩამოყალიბებული დაავადების ძირითადი დამახასიათებელი ანამნეზური, კლინიკური და დიაგნოსტიკური კრიტერიუმები. წარმოდგენილია დაავადების მკურნალობის სხვადასხვა სქემა.

PRESENCE OF PRENATAL MATERNAL STRESS INCREASES THE RISK OF THE DEVELOPMENT OF ADHD SYMPTOMS IN YOUNG CHILDREN

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Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder, with a prevalence of around 7.2% in children [1]. ADHD is characterized by symptoms of inattention, hyperactivity and impulsivity, and is associated with psychosocial impairment, poor academic functioning and psychiatric problems in children and adolescents [2]. Twin studies have shown that ADHD is highly heritable, but 10-40% of the variance in liability is explained by environmental influences [3]. In addition, the heritability estimate may include unknown amounts of environmental influences due to gene-environment interaction, and it is important to identify environmental risk

factors for ADHD, as these factors may represent targets for prevention.

Prenatal influences have received increasing attention as potential causes of ADHD [4], mainly due to the hypothesis that prenatal exposures predispose individuals to disorders such as ADHD through fetal programming. Fetal programming refers to a process where factors in the intrauterine environment are hypothesized to influence the normal development of the fetus. Prenatal exposures, such as maternal stress, might permanently influence the structure, physiology and metabolism, causing long-lasting changes that might predispose individuals to later disorders [5].

The mechanism by which maternal stress causes developmental problems in offspring is still unclear, but several hypotheses exist.

Different stressors, such as adverse life events, have been used to measure prenatal and early childhood exposure to stress. In a pioneer study from some researchers showed that aggregated psychosocial adversity was associated with an increased risk of childhood mental disorders [6], which has later been supported by several more recent studies [7,8]. However, in this study, we focus on exposures during the prenatal period in order to explore the fetal programming hypothesis. There are several studies showing an association between stressful life events during pregnancy and offspring ADHD [9-12]. However, two studies did not find any statistically significant associations between adverse life events during pregnancy and offspring ADHD [13,14].

It is important to consider the mother's subjective experience of adverse life events as the same event might be perceived as very stressful for one individual, and not stressful for another. If prenatal stress has a programming effect on the fetus, the effect may be stronger if the mother perceived the event as stressful. The mother's perception of the events has only been considered in five previous studies in relation to offspring ADHD symptoms [10,12,14-16]. One of them [10] found that prenatal exposure to high levels of stress was consistently associated with high levels of hyperactivity symptoms in 10,184 children followed from age 7 to 16. And other [12] found that severe stress during pregnancy was associated with higher odds of having elevated levels of ADHD symptoms among offspring boys (OR: 2.41, 95% CI: 1.03–5.66) but not girls (OR: 1.33, 95% CI: 0.47–3.83), based on 1,765 four-year-old children.

We aimed to clarify if prenatal exposure to adverse life events within the family is associated with the risk of developing ADHD symptoms in childhood, and if such an association remains when adjusting for familial confounding (genetic and environmental).

Material and methods. The samples included 200 children , 100 controls and 100 cases. Study participants were selected through target selection. The data had been collected in "Academician K. Nemsadze Pediatric Clinic :Globalmed" where National Center For disease and Public Health control of Georgia carried out subcomponent of the state program " early detection of diseases and screening" (01/03/2016 to 31/12/2016) . The goal of this study was to prevent, early diagnose and the elaboration of moderate and mild mental development in children of 1 to 6. Identification/screening of beneficiaries was carried out by the neurologist and neuropsychologist.

For the study group there were the following inclusion criteria:

- The diagnosis of proved attention deficit and hyperactivity syndrome.
- Informed consent of parents

For the control group there were the following inclusion criteria:

- Healthy children without neuropsychological disorders
- Informed consent of parents

We also excluded children with a history of Tourette syndrome, pervasive developmental disorder, psychosis or any medical condition interfering with their capacity to participate in the program.

For the mothers of both groups in order to study pregnancy course retrospectively we used the following exclusion criteria: medical risk-factors, such as acute and chronic diseases, especially gestational diabetes, familial case of fat metabolism disorder, arterial hypertension, hyperthireosis; first pregnancy after the age of 40; gestosis; existence of fetal development defects; psychiatric disorders. Exclusion criteria were checked during the first structural interview by neurologist and neuropsychologists.

In both groups we used a specially developed modified questionnaire including the questions about the pregnancy course, medications taken, the nature of nutrition, passive smoking, tobacco and alcohol use, demographic, economic and psycho-social status of the family, educational level and professional activity during pregnancy, also delivery type, infant weight and heigh at birth, feeding duration.

In addition to this we took into consideration daily events they could experience during pregnancy, difficulties at work/college, financial problems, divorce, split with partner, problems with family members, friends, relatives, neighbors, serious disease or self-injury or someone close people, serious accident, fire or robbery; or loss of someone close.

Through this questionnaire we investigated the effect of cumulative exposure separately for life events considered as dependent (problems at work or school; financial problems; divorce, separation, or end of a relationship; problems with family, friends or neighbors) and independent (serious illness or injury; someone close seriously ill or injured; serious accident, fire or robbery; or loss of someone close), based on categorizations used in previous studies [17-19]. All dependent events were given a value of 0 (not having experiencedthe event) or 1 (experienced the event), which were summarized into a three-level categorical variable, with levels 0, 1, and ≥2 events. A variable measuring cumulative exposure to independent life events was created in a similar manner, with levels 0, 1, and ≥2 events.

We diagnosed attention deficiency hyperactivity syndromes in children based on the criteria determined by DSM-IV-R-is (ICD 10) using of which we evaluated the tendencies of hyperactivity, impulsivity and inattention in the children of age of 1 to 6. If the evaluation met 6 or more criteria the existence of deficient functioning suspected. The above mentioned approached is used in previous studies as well. The diagnosis was based on a clinical evaluation with the family, observation of the child and a clinical interview of the parents that used the Diagnostic Interview Schedule for Children Version IV (DISC-IV),

Then we diagnosed the beneficiaries participating in state program according to ICD 10, the control group-healthy contingent was granted diagnosis Z03-Encounter for medical observation for suspected diseases and conditions ruled out, while the study group, which was diagnosed with ADHD, was categorized into 3 groups: F90.0Attention-deficit hyperactivity disorder, predominantly inattentive type, F90.1 Attention-deficit hyperactivity disorder, predominantly hyperactive typeF90.2-Attention-deficit hyperactivity disorder, combined type.

The data were processed via different methods of descriptive and inferential statistics using SPSS statistics 23.0. The proper distribution of the data was checked by using Kolmogrov-Smirnov and Shapiro-Vilki tests, Means within the group were compared via t criterion for independent selection. Intergroup comparisons for independent selection were evaluated via nonparametric Mann–Whitney U test and Kruskal–Wallis **and Jonck**-heere-Terpstra tests. Intragroup comparisons were evaluated viaChi-square tests and Fisher exact test. In order to determine the depth of correlation we used Cramer's V. In order to study linear relationship between interval variables in general population and between groups we used Pearson's correlation coefficient. And to study monotonic relationship between interval variables we used Spearman Rank coefficient. In order to determine linear relationship between some variables we used linear regression model. While to check their value we used well-known F test and t test.

Results and discussion. Cases based on diagnosis were distributed as follows: Z03 (Z03- Encounter for medical observation for suspected diseases and conditions ruled out) - 100%, F90.0 (Attention-deficit hyperactivity disorder, predominantly inattentive type) – 53%, F90.1 (Attention-deficit hyperactivity disorder, predominantly hyperactive type) – 9% and F90.2 (Attention-deficit hyperactivity disorder, combined type) – 38% (Fig. 1).

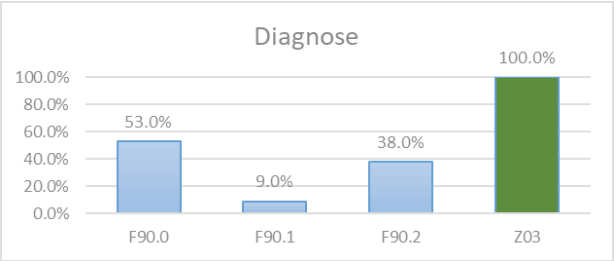

Fig. 1. Diagnose

Child's age in neuropsychological assessment and diagnosing: control group [M]±[SD]:2.88±1.33; study group: [M]±[SD]:3.50±1.21 years.

Mothers age at the time of childbirth:control group [M]±[SD]:28.02±5.30;studygroup:[M]±[SD]:26.39±5.15

Mothers' education: control group 15% secondary education, 85% - higher education, study group: 29% had secondary education, 73% had higher education.

Mothers family status at the time of pregnancy: control group - 95% were married, 5% were divorced, study group - 90% were married, 10% were divorced. Parity: control group - I pregnancy 44%, II 33%, III and more 23%, study group - I preganancy 56%, II 27%, III and more 17%. Delivery sequence: control group - I delivery 51%, II 38%, III and more 11%. Study group - I preganancy 62%, II 29%, III and more 9% (Fig. 2).

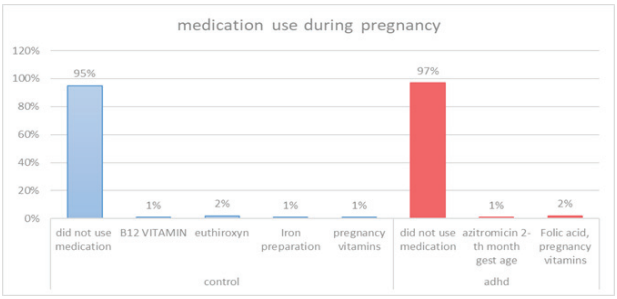

Fig. 2. Medicines taken during pregnancy

Tobacco and alcohol consumption/passive smoking during pregnancy is equal in both groups 14%: control group – only 2 was consuming. Family economic status: control group - 3% was low, 90% middle, 7% high status, study group: 11% was low 83% - middle, 6% high. Ninety-eight percent in both groups the pregnancy was wanted. 1% was unwanted. For study group mothers 70% pregnancy was planned,30% was unplanned. For study grup 89% pregnancy was planned,11% was unplanned.

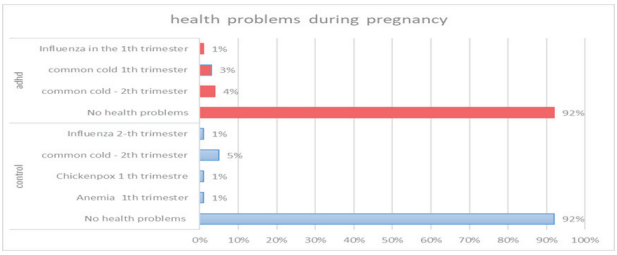

Fig. 3. Health problems in pregnancy

The frequency of professional activity of mothers during pregnancy was almost identical for both groups: 65% were working, 35% were unemployed. The distributions of children according to the sex: in control group - 40 girls, 59 - boys, in study group - 33 girls and 67 boys. The weight at birth: control group [M]±[SD]: 3281±558 g; study group: [M]±[SD]:3315±500 g. The length of the baby at birth: control group - [M]±[SD] 49.96±3.78 cm, study group - [M]±[SD] 50.14±2.83 cm.

Delivery week: control group [M]±[SD]:38±2.061 week, study group :[M]±[SD]:38±1.15 week. In 42% of control group cesarean section was performed, 58% delivery was physiological. In 51% of the study group cesarean section was performed, 49% delivery was physiological. The problems at the birth of the child for both groups was identical: 5%asphyxia, 1% was premature, 3% prolonged Jaundice. The duration of breastfeeding: control group -[M]±[SD]:7.368±8.126 months. Breastfeeding was not performed in 25%, in study group -[M]±[SD]:5.69±6.3 months. Breastfeeding was not performed in 26%.

Degree of stress: in 81% of the control group no stress was revealed, in 8% stress was moderate, and in 11% severe stress. In 46% of the cases no stress was revealed, in 33% stress was moderate, and in 21% severe stress was revealed. Stress factors-live events distribution in dependent and independent factors according to groups: 11% of the control group was dependent, whilst 8% was independent, 33% of the study group was dependent, whilst 21% was independent.

The difference between the following variables: by 95% significance, mother's age at the birth of child is more in control group mothers ([M]±[SD]:28.02±5.31 years compared with study group mothers, ([M]±[SD]:26.39±5.15 years.

Control group mothers were breastfeeding [M]±[SD]:7.36±8.12 months for longer compared with study group mothers, [M]±[SD]:5.69± **6.26 years. Al**though according to independent sample test, statistically significant difference was not revealed since this difference was proved by only 10% level of importance.

According to independent test samples, statistically significant difference was revealed between children ages on diagnosing. In particular, t(193.385)=-4.054, p<.001, control group [M]±[SD]:2.72±1.443 year,study group –[M]±[SD]:3.49±1.235 year. Study group children are older than control group ones.

Using nonparametric Mann Whitney U Test the same tendency was revealed except for breastfeeding, p<.001.

The interrelationship between categorical reliable was checked by Kruskal-Wallis Test. Thus, by p=0.001 value level, it is statistically important the correlation between diagnosis and child's age, at the time of diagnostics x^2=16.677, df =3, p=.001.also the correlation between diagnosis and maternal age. At the time of child's birth. x^2=16.017, df =3, p=.001. also, no statistically important relationship between the mentioned indices and stress level is proved. As in one case p=.065, whilst in another case p=.752

The qualitative division of stress caused differences also between thevariablesof birth weight and breastfeeding duration. In particular, as the degree of stress increases, the weight of child's weight and the duration of breastfeeding decreases.

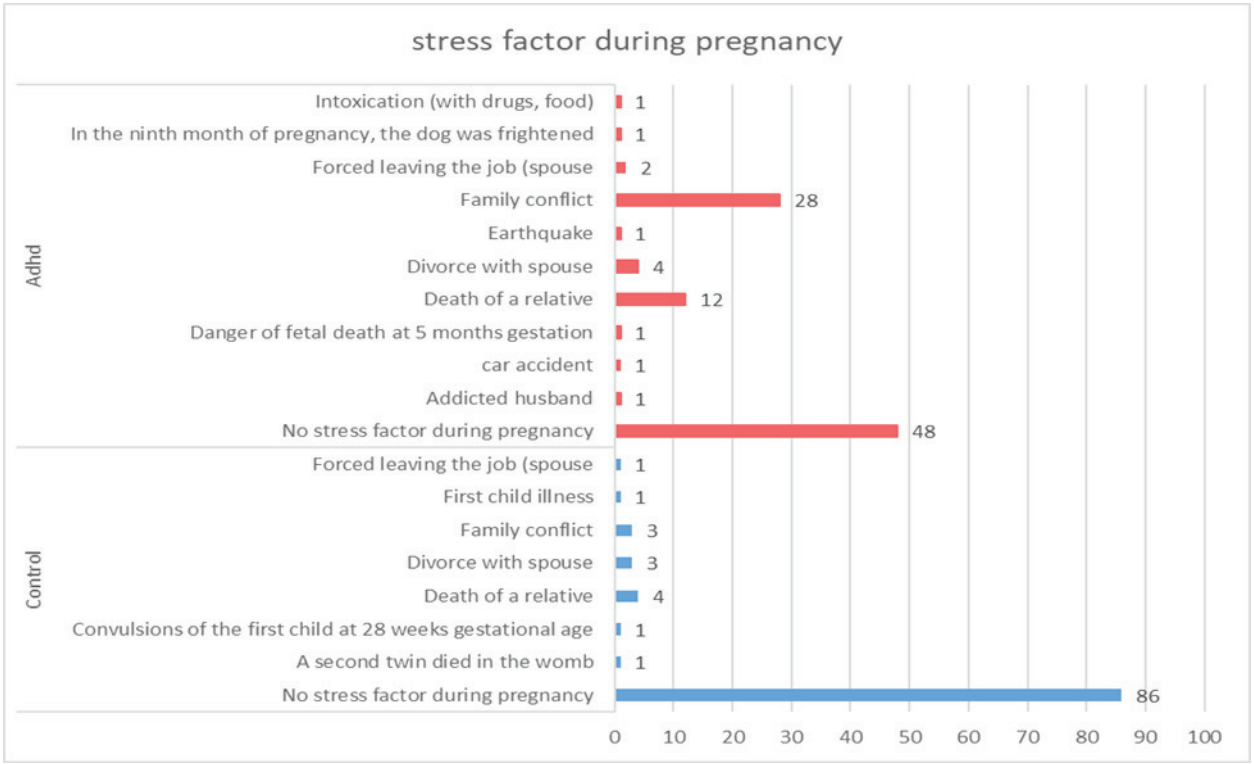

Fig. 4. Stress factors in pregnancy

*Table. Relationship between stress **degree**, body weight and duration of breastfeeding*

Stress degree	Birth Weight in g[M]	Duration of breastfeeding in month [M]
None stress	3353	7.0
Moderate stress	3265	6.01
Severe stress	3121	5.0

Using nonparametric independent sample **Jonckheere-Terpstra** Test statisticaly significant correlation was proved between stress degree and child's low birth weight, p=0.053.

In cases, by using the same test, statisticaly significant correlation was found between birth weight and stress degree, also between birh length and stress degree p=0.049 and duration of breastfeeding p-0.047.

By using Cramer V test we could not reveal important associations between socio-demographic variables and developed diagnosis. Although statistically significant correlation was established among planned/unplanned pregnancy x^2 = 11.075, df=1, p =.001 Cramer's V=.235; stress factor identification (existence/non-existence) x^2 = 26.426, df=1, p =.001Cramer's V=.364 (which confirms the strength of their correlation>0.25; stress degreex^2 =28.015,df=2, p=.001Cramer's V=.374; life events (independent events prevail) x^2 = 26.473, df=2, p=.001, Cramer's V=.364 and existed diagnosis.

Correlated analysis was performed using Pearson's correlation coefficient and Spearman's rank correlation coefficient. For general population, using Pearson's coefficient, statistically significant linear correlation was established: mother's age positively correlates with pregnancy sequence at the time of diagnostics of a childp<.001, also significantly correlates child's birth weight p<.05. Birth weight significantly correlates with pregnancy sequence p< .05, birth length and birth week p< .001. Birth week positively correlates birth weight and birth length p< .001.Using nonparametric, correlation test, Spearman's rank correlation coefficient, and the same tendency was revealed, here we encounter monotonic relation, no linear. Using this test we observed statistically significant relationship between family status during pregnancy (married/divorced) and the identification of stress factor (existence/non-existence) for general population and not separate was observed between existence of stress as a factor and already existed diagnoses x^2=26.426, df=1, p=001 Cramer's V=.364 (which proves the strength of their connection V>0.25). Stress factor playsan important role in the development/non-development of the syndrome. But it does not give us any significant information which type of syndrome will be developed:F90.0 , F90.1, F90.2: x^2=2.660, df =2, p=258 Cramer's V=.163.We also studied whether there was a statistically significant relationship between diagnoses (F90.0, F90.1 da F90.2) and stress degree which was not proved using Chi-square. As regards the study of the relationship of stress factors (dependent./independent, where independent factors prevail independent factors) with the given diagnoses using chi-square test, no statistically significant relationship was determined x^2=.061,df=1,p=1.000 Cramer's V=.029. We also studied the relationship between stress degree (moderate/severe) and life events (dependent/independent) .we revealed that moderate degree of stress is determined dependent reasons. Severe stress is determined by independent stress factors. this relationship is statistical significant and strong x^2=41.028 , df=, p=001 Cramer's V=.750.

In order to study the impact of newborn infant length and diagnoses on birth weight we used regression analyses. As a dependent variable newborn length and diagnoses were used, besides, we built up the models for weight and length for separate groups.

According to the gained result in both models birth weight is significantly correlated with birth weight and diagnosis. In one case the coefficient of determination R2 is 0.417.

In order to determine the reliability of obtained result we used multifactorial dispersion analysis ANOVA method. This method revealed that the difference between mean values of dependent and constant variables was not statistically significant F=114.779 p<0.001. in both cases the model is statistically significant. For birth length ß=-116t(199)=-6553 p=0.001. as the model is one-factor the variable of the model is statistically significant using t test.

In order to study the impact of newborn length and maternal stress on newbornweight , we still used regression analysis. AS an independent variable we considered newborn weight, as dependent variables we considered newborn length and prenatal stress as an actual variable. According to the obtained result newborn weight is significantly related to newborn length and prenatal stress, that is the model is statistically significant, determination coefficient is R2 = 0.546. As regards the variables, newborn length is statistically significant by even 1% value level,while stress identification actual variable by 10% value.In order to study the impact of newborn length and stress degree on newborn weight, we still used regression model. As a dependent variables we used newborn length and stress degree. By the obtained result, newborn weight is significantly correlated with newborn length and prenatal stress degree R2 = 0.547..In order to determine the significance of regression analyses we still used ANOVA method. Which revealed statistically significant correlation between mean values of dependent and constant variables. F=78.812 p<.001. For the length at birth ß=114,.971t(199)=-15.011 p=0.001. For moderate stress ß=-73.810 t(199)=--1.144 p=0.001. For severe stress ß=

- 127.510 t(199)=-1.787 p=0.001.Consequently these factors are interrelated and their interaction effect is high.

In order to determine the correlation between stress and diagnose we used the simplest logistic regression, where we consider stress existence/nonexistence as a dependent variable. By using this model the correlation between them is statistically significant p=.001. In case of stress the ratio of the development of the syndrome and underdevelopment of it increases by 5 fold odds Ratio=5. We also determined the relative risk of the development of attention deficiency and hyperactivity syndrome in case of stress existence and non-existence. Which revealed that the risk of the development of stress in the children of stress experienced mothers for our study population in 2 fold higher than the risk of the children of stress free mothers RR =2.042

The focus of this study was on investigating the association between prenatal maternal stress and child ADHD symptoms in early childhood (1 to 6 years) in the offspring. The main objectives were to examine whether prenatal stress exposure is associated with higher levels of child ADHD symptoms, and whether the strength of the association differs according to the timing of the stress exposure. This study is unique in that the associations were investigated controlling for a wide array of covariates, in Georgia among the studies related to ADHD. Besides, we studied the impact of some specific life events.

Based on the results pained by us, prenatal maternal stress was significantly associated with higher levels of ADHD symptoms in the offspring. The associations were significant for stress during pregnancy overall and no for each pregnancy trimester separately or according to its degree (mild, moderate,severe). No interaction effects regarding child sex were found for the other trimesters nor for pregnancy overall. The results are in line with my hypothesis and consistent with the findings of the majority of previous studies [11,15,21,22,24,25]. Also, it is very important that stress degree during pregnancy is closely related to the weight and length of the baby at birth as well as the duration of breastfeeding. In particular, along with the increase in stress degree , baby's birth weight, length and duration of breastfeeding decrease. The findings from the current study expand the results concerning toddlers and preschoolers, showing significant associations between prenatal stress exposure and higher levels of ADHD symptoms in early childhood, in children aged one to five. This is an important finding, as early intervention has been found the most effective in preventing ADHD [26,27]. As regards the identification of stress factors, dependent life events are more heritable than independent life events [28], and thereby also more likely influenced by the individual's personality traits or genetic predisposition to ADHD. In this study, associations between adverse life events in the family during pregnancy and ADHD symptoms in offspring seemed to be stronger for dependent events (such as financial problems and separation/divorce), and weaker for independent events (e.g. bereavement and injury/ illness in someone close), indicating the presence of genetic confounding. Some limitations should be kept in mind when interpreting the results from this study. Self-selection due to low participation could have introduced bias. Selection into the cohort has been shown to influence prevalence estimates for several pregnancy- related exposures and outcomes, but not the association between these exposures and outcomes [29]. A recent Norwegian study found that families with lower socioeconomic position more frequently experience negative life events [30]. Since, early childhood exposure to financial difficulties has been associated with ADHD even after adjusting for familial factors [31], future studies are needed to investigate associations with adverse life events specificallyamong families with lower socioeconomic position to assess the generalizability of our findings. Due to the young age of study participants, and in order to increase statistical power, we relied on parent-rated ADHD symptoms instead of clinical diagnoses. However, several studies have suggested that ADHD can be viewed as a dimensional scale of symptoms [32,33]. This resulted in a smaller sample for this study, but is unlikely to influence the association between prenatal exposure to life events and ADHD symptoms.

However, parental assessment of problem behavior is a practical option for large preschool samples, and parents are familiar with behavior across time and a range of contexts. Hence, it is less assumed that it can have an impact on the associations between prenatal exposition and ADHD symptoms of life events.

The study conducted by us did not include information on the mothers' subjective experience of the stressors. There is some evidence that objective measures of stress are better than subjective measures at predicting later child outcome [34].

The findings suggest that intervention that seeks to minimize the number of stressors that a woman experiences during pregnancy could have an effect to reduce the risk of the offspring developing ADHD-like behaviors. These results lay the foundations for future research using epigenetic, cross-fostering, and gene–environment interaction designs to identify the causal processes underlying these associations.

Conclusion. The findings suggest that the prenatal stage of a child's life seems to be very important in terms of his or her development and support the hypothesis that prenatal stress causes offspring ADHD through a programming effect and future research should focus on exploring other prenatal influences that might be causally related to ADHD.

Consequently it is extremely important to take care of and support pregnant women because this may decrease their child's chance of developing ADHD and other symptomatology.

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SUMMARY

PRESENCE OF PRENATAL MATERNAL STRESS INCREASES THE RISK OF THE DEVELOPMENT OF ADHD SYMPTOMS IN YOUNG CHILDREN

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Aims - to identify association between maternal stress during pregnancy and the developemnt of the attention deficiency hyperactivity syndrom in young children

We conducted a case-control study sequentially recruiting 200 children from the "Early detection of disease and screening" State Program, from them 100 children with ADHD diagnose, and 100 subjects, as a control group, without Disruptive Behavior Disorder (DBD), aged between 1 and 6 years. The children were diagnosed with ADHD according to the DSM-IV-R and a clinical interview of the parents that used the Diagnostic Interview Schedule for Children Version IV (DISC-IV). We investigated the effect of cumulative exposure separately for life events considered as dependent and independent.The mother's stress level was scored from 1 to 5 on the DSM-III and DSM-III-R axis IV scales, according to the highest level of stress experienced during the pregnancy.

The presence of stress factor plays an important role in the development of ADHD syndrome, but does not play a statistically significant role in which type of syndrome develops: F90.0, F90.1, F90.2: p=.258. A statistically significant relationship between ADHD diagnosis and stress degree was not confirmed at p=.503. Our data revealed that moderate-grade stress is caused by dependent causes, severe stress by independent causes, this association is statistically significant(p=.001 Cramer's V=.750). A statistically significant negative association was also found between the presence of prenatal stress and the length and weight of the baby at birth. For our study population, the risk of developing the syndrome in children of stress-relieved mothers was 2 times higher than in children of non-stressed mothers RR = 2.042.

These findings show that there is an association between maternal stress during pregnancy and ADHD symptoms in offspring and support the hypothesis that prenatal stress causes offspring ADHD through a programming effect and future research should focus on exploring other prenatal factors that might be causally related to ADHD.

Keywords: fetal programming, attention deficit hyperactivity disorder (ADHD), prenatal stress.

РЕЗЮМЕ

ПРЕНАТАЛЬНЫЙ МАТЕРИНСКИЙ СТРЕСС УВЕЛИЧИВАЕТ РИСК РАЗВИТИЯ СИМПТОМОВ СИНДРОМА ДЕФИЦИТА ВНИМАНИЯ И ГИПЕРАКТИВНОСТИ У ДЕТЕЙ РАННЕГО ВОЗРАСТА

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Цель исследования - определить связь между материнским стрессом во время беременности и развитием синдрома дефицита внимания и гиперактивности у детей раннего возраста. Проведено

исследование случай-контроль, в которое последовательно включены 200 детей в возрасте от 1 до 6 лет из Государственной программы «Раннее выявление заболеваний и скрининг», из них 100 детей с диагнозом синдрома дефицита внимания и гиперактивности (СДВГ) и 100 в качестве контрольной группы без деструктивных расстройств поведения (ДПР). Детям поставлен диагноз СДВГ в соответствии с Диагностическим и статистическим руководством по психическим расстройствам (DSM-IV-R) и клиническим опросом родителей с использованием Графика диагностических интервью для детей версии IV (DISC-IV). Исследован эффект кумулятивной экспозиции на отдельные жизненные события, зависимые и независимые. Уровень стресса матери оценивался от 1 до 5 баллов по шкалам DSM-III и DSM-III-R оси IV в соответствии с самым высоким уровнем стресса, пережитого во время беременности.

Выявлено, что наличие фактора стресса играет значимую роль в развитии синдрома СДВГ, однако статистически значимого влияния на тип синдрома (F90.0, F90.1, F90.2) не установлено (p=0,258). Статистически значимая связь между диагнозом СДВГ и степенью стресса также не подтверждена (p=0,503). Полученные статистически значимые данные показали, что стресс умеренной степени вызван зависимыми причинами, тяжелый стресс - независимыми причинами (p=0,001, V Крамера=0,750). Статистически значимая отрицательная связь выявлена между наличием пренатального стресса и ростом и весом ребенка при рождении. В исследуемой популяции риск развития синдрома у детей матерей, подвергшихся стрессу, был в 2 раза выше, чем у детей матерей без стресса (RR=2,042).

Полученные в результате исследования данные указывают на наличие связи между стрессом у матери во время беременности и симптомами СДВГ у потомства и подтверждают гипотезу, что пренатальный стресс вызывает СДВГ за счет эффекта программирования. Авторы считают целесообразным проведение исследований в будущем по изучению других пренатальных факторов, причинно связанных с СДВГ.

რეზიუმე

დედისმიერი სტრესის არსებობა ორსულობის დროს ზრდის ყურადღების დეფიციტის და ჰიპერაქტიურობის სინდრომის განვითარების რისკს მცირე ასაკის ბავშვებში

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კვლევის მიზანს წარმოადგენდა დადგენილ იქნას დედისმიერი სტრესი ორსულობის დროს ასოცირებულია თუ არა ყურადღების დეფიციტისა და ჰიპერაქტიურობის სინდრომის განვითარებასთან უმცროსი ასაკის ბავშვებში.

ჩატარდა **შემთხვევა-კონტროლის კვლევა, რო**მელშიც ჩართული იყო 1-დან 6 წლამდე 200 ბავშვი, 100 ბავშვმა მენტალური და ქცევითი დარღვევების გარეშე შეადგინა საკონტროლო ჯგუფი, **საკვლევი ჯგუფი - 100 ბავშვი დადა**სტურებული ყურადღების დეფიციტის და ჰიპერაქტიურობის სინდრომის (ADHD) დიაგნოზით. კვლევაში **მონაწილე სუბიექტთა შერჩევა გან**ხორციელდა **მიზნობრივი შერჩევის გზით, სა**ხელმწიფო პროგრამის „დაავადებათა ადრეული გამოვლენა და სკრინინგის“ ქვეკომპონენტის ფარგლებში მიღებულ მასალაზე დაყრდნობით. ბავშვებში ADHD-ის დიაგნოსტირება მოხდა DSM-IV-R-ის **მიხედვით, განსაზღვრული კრიტე**რიუმების და მშობლების კლინიკური ინტერვიუს **საფუძველზე, გამოყენებული იყო ბავშვების**თვის განკუთვნილი დიაგნოსტიკური ინტერვიუ, ვერსია IV (DISC-IV). **გამოვიკვლეულია კუმულა**ციური ექსპოზიციის ეფექტი ცხოვრებისეულ მოვლენებზე, რომლებიც განიხილება, როგორც დამოკიდებული და დამოუკიდებელი მოვლენები. დედის სტრესის დონე განისაზღვრა DSM-III და DSM-III-R ღერძის IV შკალებით, სადაც სტრესის დონე შეფასდა 1-დან 5 ქულამდე, **რაც ორსუ**ლობის დროს გადატანილი სტრესის უმაღლესი ხარისხის შეფასებას ემსახურება.

სტრესის ფაქტორის არსებობა მნიშვნელოვან როლს ასრულებს ADHD-ის **განვითარებაში, მა**გრამ **არ თამაშობს სტატისტიკურად მნიშვნელო**ვან როლს, თუ რომელი ტიპით განვითარდება სინდრომი: F90.0, F90.1, F90.2, p=.258. სტატისტიკურად მნიშვნელოვანი კავშირი ADHD დიაგნოზსა და სტრესის ხარისხს შორის არ დადასტურდა, p=.503. მონაცემებმა გამოავლინა, რომ საშუალო ხარისხის სტრესი გამოწვეულია დამოკიდებული, ხოლო მძიმე კი - დამოუკიდებელი მოვლენებით და **ეს ასოციაცია სტატისტიკურად მნიშვნელო**ვანია (p=.001 Cramer’s V=.750). სტატისტიკურად უარყოფითი **კორელაცია გამოვლინდა ასევე პრე**ნატალურ **სტრესსა და ბავშვის დაბადების წო**ნასა **და სიგრძეს შორის. საკვლევი პოპულაცი**ისთვის პრენატალური სტრესის მქონე დედების შვილებში ADHD-ს განვითარების რისკი 2-ჯერ

მეტია სტრესის არამქონე დედების შვილებთან შედარებით (RR=2.042).

მიღებული შედეგები ადასტურებს ჰიპოთეზას, რომ **პრენატალური სტრესი იწვევს შთამომავლობაში** ADHD-ს განვითარებას პროგრამირების ეფექტის **მეშვეობით. გამომდინარე ზემოაღნიშნულიდან, სამომავლო კვლევები მიზანმიმართული** უნდა იყოს სხვა პრენატალური ფაქტორების ზემოქმედების შესწავლაზე, რაც შესაძლებელია გახდეს ADHD-ს განვითარების მიზეზი.

IMPACT OF MICROBIOME COMPOSITION ON QUALITY OF LIFE IN HEMODIALYSIS PATIENTS

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Chronic Kidney Disease (CKD) represents a great challenge for the whole world. Worldwide, approximately 242/1,000000 patients with CKD (The global estimated prevalence is 13.4% (11.7-15.1%) and the number of patients with kidney failure is expected to increase [1;2]. During the last years, the share of dialysis programs in health financing has increased from 6% to 12% especially, in developed countries and still proceeds to grow [3]. According to the official data of 2021, 2670 people, 716 out of the million-population received Kidney Replacement Therapy (KRT) in Georgia, with an average age of 58.4. The lack of a cadaver kidney transplant program in Georgia increases the vintage of the patients on dialysis. Long-term dialysis therapy often results in an increased risk of systemic inflammation.

Chronic inflammation in the CKD population can have a serious impact on patients' quality of life (QoL) [4-6]. Markedly altered intestinal flora plays an important role in the increased production of gut-derived uremic toxins such as indoxyl sulfate and p-cresol sulfate, promoting pro-inflammatory responses [7,8]. Systemic inflammation increases with the progression of CKD. Despite appropriate treatment with KRT, systemic inflammation may dramatically change the psychological, social, economic prosperity of hemodialysis (HD) patients [9]. Thus, intestinal microbiome disturbances may lead to serious changes in HD patients' QoL. The potential benefit from modulating the "healthy" colonic colonization may become improvement of QoL of this population.

The aim of our study was the assessment of QoL of the HD patients before and after therapy with refined probiotics. The Missoula-VITAS Quality of Life Index (MVQOLI) was used for this purpose. The MVQOLI evaluates 5 dimensions of patients' QoL: symptoms, function, interpersonal, well-being, and transcendence [10]. The questionnaire is specifically designed to assess the patients' personal experience in each of these dimensions. It is important to mention that factors that influence QoL in patients with kidney failure receive little attention

Material and methods. In this cohort-prospective study we included 272 patients on maintenance hemodialysis from a single-center loaded with 300 regular HD patients. All patients were on the same regime range of 12h per week with a mean single pool of Kt/V 1.55 [interquartile range IQR 1,45-1.65]. The median age of the patients was 54 [IQR, 44-68], sex distribution 160 men (57%) and 112 women (43%), and a dialysis vintage 3 years [IQR 3-7]. The study was designed as a two-step approach: the first step aimed the assessment of overall QoL of the HD patients and selection of those with gastrointestinal complaints – forming of the "GI group"; the second step included the fecal investigation and probiotic treatment of the patients from the "GI group" followed by reassessment of QoL by the end of the treatment. Initially, we used two questionnaires: the first - the Missoula-VITAS Quality of Life Index-15 (MVQOLI-15) translated into Georgian; the second - related to gastroenterological complaints. The purpose of the questionnaire was to reveal the number of patients with gastrointestinal complaints, and the severity of these symptoms. The second step of the study focused on the effect of probiotics on the quality of life of HD patients. HD patients were eligible to participate in the study if none of the following conditions were met: HD duration ≤3 months, active inflammatory diseases, bleedings and other chronic gastrointestinal diseases, viral hepatitis, severe mental and oncological diseases in past medical history. We have selected 33 patients for the "GI group" with mean age of 30 (IQR 18-65) and sex following distribution - 17 females and 16 males. Each patient has been studied under an individual schedule, the same scheme, for 12 weeks. We have studied intestinal flora, quality of life, and gastrointestinal complaints before and after treatment. Also, 7 HD patients were recruited as the control group with no gastrointestinal problems. All participants were informed about the research purposes. The patients included in the study have signed informed consent.