SPECIJALNA EDUKACIJA I REHABILITACIJA
2022, Vol. 21, Br. 3, str. 163-176
UDK: 616.896(497.7)
Originalan naučni rad
DOI: https://doi.org/10.5937/specedreh21-36888

The importance of early diagnosis of autism spectrum disorder for adequate treatment and rehabilitation in Macedonia

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Introduction. Autism spectrum disorder (ASD) has unclear etiology and no known universal treatment, making it difficult to obtain an accurate and timely diagnosis. The evidence that highlights the importance of early diagnosis and treatment is growing. *Objective*: The research was done to evaluate the impact of early diagnosis and its significance, as well as the effectiveness in obtaining the diagnosis in the past years and decades in Macedonia. *Methods.* We carried out a comparative analysis of the collected data from 95 subjects divided into three groups: 30 parents, 35 special educators and rehabilitators, and 30 members of the professional team that participated in diagnosing autism, using an original research tool in the form of three questionnaires. The data from the study refers to a research study conducted in Macedonia. *Results.* Many prenatal, perinatal, and postnatal factors can lead to ASD. The most common symptoms include: lack of speech, delayed speech for a specific age, not responding to their name, no eye contact, weak social skills, hyper/hyposensitivity, and isolation. Autism more frequently occurs isolated than accompanied by other conditions. The mean age of diagnosis used to be 5.6, while, in recent years, it has been 4.2. Children wait around 2.1 years from the first symptoms to obtain a diagnosis. Parents visit fewer institutions in the process of obtaining an ASD diagnosis. There is still a significant number of misdiagnoses. *Conclusions.* Many factors play a role in the occurrence of autism. There are a number of symptoms that appear in most cases. In the last decade, autism has been diagnosed earlier than before. The approach and process of diagnosing autism in Macedonia have improved.

Keywords: autism spectrum disorder, early diagnosis, treatment, rehabilitation

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Note. This paper is part of a graduation's thesis Petrusheva, T. K. (2021). Rana i ispravna dijagnoza kao ključni deo odgovarajućeg lečenja i rehabilitacije osoba sa autizmom [Early and correct diagnosis as a key part for appropriate treatment and rehabilitation for people with autism] [Unpublished graduation's thesis]. "Ss. Cyril and Methodius" University Skopje.

Introduction

Autism spectrum disorder (ASD) is still a condition of unknown etiology. As a result, it cannot be detected through genetic testing and medical tests. Therefore, greater emphasis is placed on the early detection of specific symptomatology.

Despite a significant increase in the number of ASD diagnoses over the past decades, which has indicated that this life-long neurodevelopmental disorder affects around 1–1.5% of the general population, making ASD a relatively common disorder, the topic of missed diagnoses and misdiagnoses continues to be an important issue (Schilbach, 2022).

Even with extensive research and greater public awareness, ASD has an unclear etiology and no known universal treatment, making it difficult to obtain an accurate and timely diagnosis. The evidence that highlights the importance of early diagnosis and treatment is growing, which can significantly improve the quality of life of people with ASD, their caregivers, and families.

Numerous studies show that children with ASD, thanks to early intervention, have positive outcomes in cognitive and adaptive functioning (Reichow et al., 2018; Remington et al., 2007; Zachor et al., 2007).

One study shows that children with ASD who were diagnosed earlier exhibited a larger reduction in the severity of social ASD symptoms within 1–2 years. Specifically, children diagnosed before 2.5 years of age were nearly three times more likely to exhibit considerable reductions in the severity of social symptoms compared to children diagnosed at older ages. Equivalent results were evident when examining boys and girls, suggesting that boys and girls benefit similarly from early diagnosis. These findings reveal that ASD diagnosis before the age of 2.5 is associated with considerable improvement in social symptoms. Greater brain plasticity and behavioral flexibility enable younger children to benefit more from ASD interventions, even in community settings with heterogeneous services. This motivates further prioritization of early ASD screening (Gabbay-Dizdar et al., 2021).

Through early diagnosis, parents of autistic children can learn how to help their child progress mentally, emotionally, and physically during developmental stages with the help of professionals. Finally, the discovery of ASD and the early handling of the situation also benefit the relationship between parents. Exhaustive care for an autistic child can be a daily challenge for them, but with early diagnosis and intervention, parents can prepare emotionally and mentally to deal with specific situations.

In Macedonia, only physicians (psychiatrists and pediatricians) are allowed to diagnose autism officially. There is a lack of knowledge on ASD among professionals involved in working with children with ASD and a lack of standardized protocols for early detection, diagnosis, and assessment tools. The precarious use of international classifications and diagnostic tools results in low

and late detection of autism. There is still no national strategy for ASD in the country (Trajkovski, 2017).

In Macedonia, this particular kind of research has not been done so far. This topic has importance for future diagnostic practices leading to earlier detection and timely and accurate diagnosis. It is an example of the ASD recognition state from a sample in Macedonia and for further comparison with practices of this kind in the world.

The aim of the research was to examine the impact of early diagnosis and its significance for successful treatment of autistic symptoms, as well as the effectiveness in obtaining the diagnosis in the past years and decades in Macedonia.

Methods

Sample

The research sample included 95 participants divided into three groups: 30 parents of children with ASD aged three to 24 years at the time of the research, 35 special educators and rehabilitators, and 30 members of the professional team that participated in diagnosing ASD (psychologist, special educator and rehabilitator, pediatrician, family doctor, speech therapist, psychiatrist, neurologist, teacher, specialist for preschool vaccination). Parental consent was obtained for the information required for the research.

The research started on 30th July 2021 and was completed on 27th October 2021. It was conducted on the territory of Macedonia, in public and private institutions, rehabilitation centers, hospitals, schools, day care centers, and online groups.

Instruments

An original research tool was created for the purpose of this research in the form of three questionnaires intended for parents who have a child with ASD, special educators and rehabilitators, and the team that participated in early detection and diagnosis in children with ASD. Each questionnaire contained 7–28 questions based on the research needs and the information we could obtain from each category of participants.

In the questionnaire intended for parents who have a child with ASD, the questions covered the parent and child's age, gender, prenatal, perinatal, and postnatal complications, when and which symptoms were noticed, how many institutions the parents visited before an accurate diagnosis, age of diagnosis, and previously made misdiagnoses.

The questionnaire intended for special educators and rehabilitators detailed the symptoms in children with ASD.

The questionnaire intended for the team participating in the detection and diagnosis of people with ASD included questions about the participant's profession,

the most common age of ASD diagnosis, which diagnostic methods and tools they most often used, the occurrence of ASD as an isolated case or with associated disorders, how often parents came with an already made diagnosis to confirm or reconsider it, and the most commonly observed symptoms.

Statistics

The data obtained from the research were grouped, tabulated, and graphically processed in the Microsoft Office Excel 2016 program. The data was processed with the online Statistical Calculator program. We used descriptive and inferential percentage displays of the given categories of answers, the Chi-squared test, and linear correlation with Pearson's coefficient. Significance was determined at the level of $p < 0.05$.

Results

The results show the factors that can lead to ASD, clinical features and comorbidity states that may occur, the age at which ASD occurs most frequently, the age of diagnosis, proper diagnosis, most commonly used diagnostic tests and procedures, and institutions parents often refer to.

According to the data obtained from the responses of parents who have a child with autism, there was a significant difference in relation to gender. ASD was more common in boys. There were 23 boys with a percentage representation of 76.7%, while in seven girls, the percentage representation was 23.3%. The ratio of male versus female was 3:1.

Table 1 shows significant risk factors according to the answers of parents who have a child with ASD.

Table 1

Risk factors associated with ASD

Risk factors	%
Genetic diseases	1.3
Mother's age > 35 years	7.7
Previous miscarriage	6.4
Paternal illnesses	1.3
Illnesses/infections during pregnancy	8.9
Medications during pregnancy	12.8
Prenatal complications	14.1
Perinatal complications	7.7
Cesarian section	15.4
Incubator/oxygen	3.9
Preterm labor	3.9
Low birth weight	5.1
Infections, diseases or injuries in the first years of a child's life	11.5

The prenatal, perinatal, and postnatal factors are thoroughly specified below.

Prenatal complications listed by parents included: antepartum hemorrhage 18.1%, diabetes 18.1%, preeclampsia 9.1%, stress 9.1%, subchorionic hematoma 9.1%, hydronephrosis 9.1%, low umbilical cord blood flow 9.1%, infection 9.1%, and prolonged leakage of amniotic fluid after amniocentesis 9.1%.

Perinatal complications listed by parents included: premature delivery 30%, oligohydramnios 20%, breech fetal position 10%, post-term pregnancy 10%, asphyxia 10%, placental abruption 10%, and failure to progress 10%.

Infections, diseases, poisoning, and physical injuries listed by the parents in the first years of the child's life included: infections 45.5%, injuries 27.2%, vaccine 18.2%, and febrile condition 9.1%.

Table 2

Comparative statistics of the most common symptoms according to the three groups of participants

Symptoms	fo	ft	fo-ft	$(fo-ft)^2$	$(fo-ft)^2/ft$
Absence of speech, late or delayed speech for a specific age	71	59	12	144.00	2.44
Not responding to their name	59	59	0	0.00	0.00
No eye contact	63	59	4	16.00	0.27
Poor social skills	60	59	1	1.00	0.02
Hyper/hyposensitivity	52	59	-7	49.00	0.83
Isolation	49	59	-10	100.00	1.69
Total	354				5.25
Chi square = 5.25		$p > .05$		$df = 5$	

Comparative statistics of the most common symptoms according to the three groups of participants showed no statistically significant difference in participants' answers at the level of significance of .05 (Chi-square = 5.25, $p > .05$, $df = 5$) (see Table 2).

Comparative analysis according to the results of parents and the professional team showed that primary ASD occurred in 57% of the participants. The remaining 43% had a secondary form of ASD with the following most common comorbidities: epilepsy 11%, attention deficit disorder (ADD) 11%, cerebral palsy (CP) 11%, intellectual disability (ID) 5%, and delayed psychomotor development 5%.

The team that participated in the detection and diagnosis of autism stated that the frequency of parents coming to confirm or reconsider the diagnosis already established elsewhere was: very common 30%, common 20%, not very common 50% (Table 3).

Table 3

How often parents come to confirm or reconsider an already established diagnosis

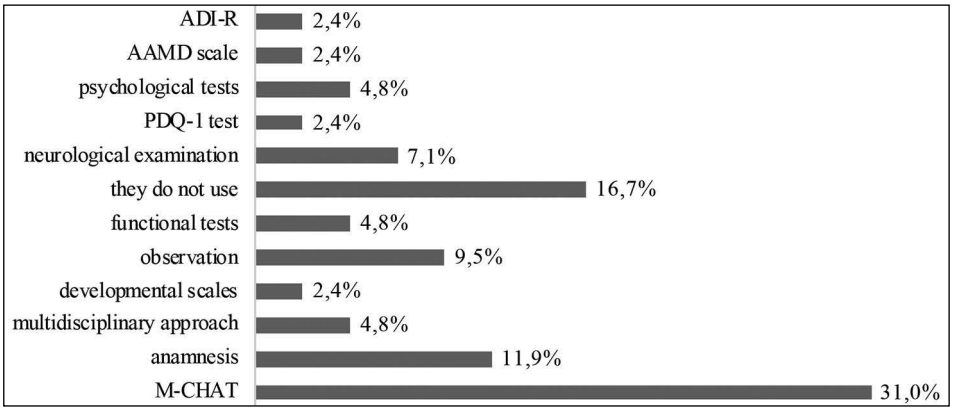
Claims of the participants	f	ft	fo-ft	$(fo-ft)^2$	$(fo-ft)^2/ft$
Very common	9	10	-1	1.00	0.10
Common	6	10	-4	16.00	1.60
Not very common	15	10	5	25.00	2.50
Total	30				4.20
Chi square = 4.20		$p > .05$		$df = 2$	

There was no statistically significant difference in participants' answers to the question *How often parents come to determine or reconsider an already established diagnosis* (Chi-square = 4.20, $p > .05$, $df = 2$).

Professionals participating in autism detection and diagnosis cited the diagnostic tests and procedures they used most often, and their responses are shown in Chart 1.

Chart 1

Most used diagnostic tests and procedures



Comparative age statistics of diagnosis according to the views of the parents and the professional team showed no statistically significant difference in participants' answers ($r = .43$, $p > .05$, df = 6) (Table 4).

Table 4

Comparative age statistics of diagnosis according to the views of the parents and the professional team

Claims of the participants	Parents	Professionals			
Age	X	У	x^2	$У^2$	XxУ
1 year	0	5	0	25	0
2 years	4	6	16	36	24
3 years	8	10	64	100	80
4 years	4	7	16	49	28
5 years	3	2	9	4	6
6 years	4	0	16	0	0
7 years	6	0	36	0	0
8 years	1	0	1	0	0
Total	30	30	158	189	138
$r = .43$		$p > .05$		$df = 6$	

A comparative analysis of the age of diagnosis was performed. Children with ASD were divided into two categories according to the year of birth: 1997–2010 and 2011–2021. In the group of children born from 1997–2010, the age of diagnosis was: seven years 20%, six years 20%, five years 20%, four years 20%, three years 13.3%, and two years 6.7%. The average age of ASD diagnosis in the first group was 5.1 years.

In the group of children born from 2011–2021, the age of diagnosis was: three years 40%, two years 20%, seven years 20%, four years 6.7%, six years 6.7%, and eight years 6.7%. The average age of ASD diagnosis in the second group was 4.2 years (Table 5).

Table 5

Comparative age statistics of diagnosis

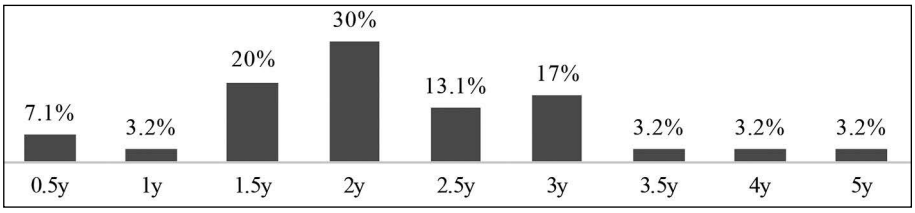
Year	1997–2010	2011–2021			
Children's age	X	У	x^2	$У^2$	XxУ
2 years	1	3	1	9	3
3 years	2	6	4	36	12
4 years	3	1	9	1	3
5 years	3	0	9	0	0
6 years	3	1	9	1	3
7 years	3	3	9	9	9
8 years	0	1	0	1	0
Total	15	15	41	57	30
$r = -.15$		$p > .05$		$df = 5$	

With regard to the comparative age statistics of diagnosis, we did not find a statistically significant difference between the two variables at the level of significance of .05 ($r = -.15$, $p > .05$, $df = 5$).

According to parents, the first symptoms were most frequently noticed at: two years 30%, one and a half years 20%, three years 17%, and two and a half years 13.1% (Chart 2). The mean value of the first observed symptoms was 2.2 years.

Chart 2

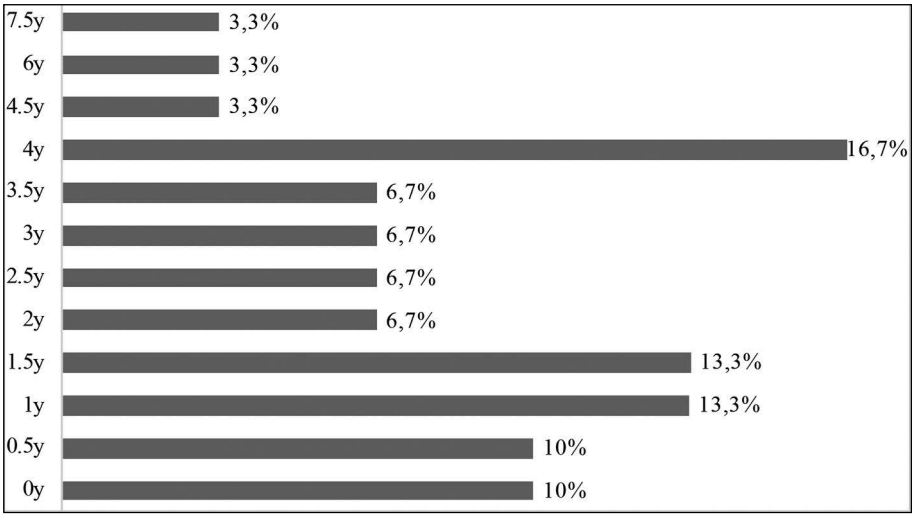
Age of the child at the first noticed symptoms



The time frame from the first noticed symptoms to the diagnosis, according to data obtained from parents of children with ASD, is shown in Chart 3. The average value of the given data indicates that 2.1 years was the waiting period from the onset of symptoms to the diagnosis.

Chart 3

Time frame from the first symptoms to the diagnosis of ASD



In relation to the process of obtaining the ASD diagnosis for children born from 1997–2010, the number of specialized institutions parents visited was: five and more than five 47%, two 27%, three 13%, one 13%. While for children born from 2011–2021, the number of specialized institutions parents visited was: two 33%, three 27%, five and more than five 27%, one 13%.

Table 6

Comparative statistics on how many institutions were visited before the diagnosis of children born from 1997–2010 and 2011–2021

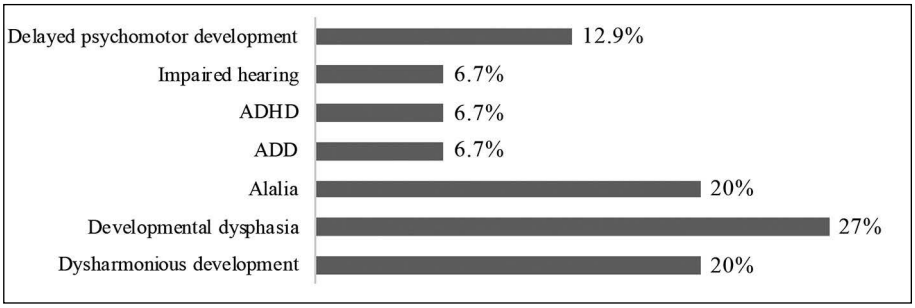
Claims of the participants	fo	ft	fo-ft	$(fo-ft)^2$	$(fo-ft)^2/ft$
A	2	0.6	1.4	1.96	3.27
B	2	0.6	1.4	1.96	3.27
C	4	4.5	-0.5	0.25	0.06
D	5	4.5	0.5	0.25	0.06
E	2	3	-1	1	0.33
F	4	3	1	1	0.33
G	7	5.5	1.5	2.25	0.41
H	4	5.5	-1.5	2.25	0.41
Total	30	27.2	2.8	10.92	8.13
Chi square = 8.13		$p < .01$		$df = 2$	

Comparative statistics on how many institutions were visited before the diagnosis of children born from 1997–2010 and 2011–2021 showed a statistically significant difference at the level of significance of .01 (Chi-square = 8.13, $p < .01$, $df = 2$). The results show that the attendance of several institutions in the period from 1997–2010 was higher compared to the period from 2011–2021 (Table 6).

According to data obtained from parents, 60% of children got a correct initial diagnosis, while the initial misdiagnosis was made in 40% of the children. Initial misdiagnoses included: developmental dysphasia 27%, alalia 20%, and disharmonious development 20% (Chart 4).

Chart 4

Misdiagnosis before the diagnosis ASD



Discussion

According to our research, ASD is more common in males in the ratio of 3:1, and the prevalence of ASD with other comorbidities is frequent (43%). The most common comorbidities included: epilepsy, ADD, CP, ID, and delayed

psychomotor development. Our results confirm the findings of Lai et al. (2014) that autism affects more male than female individuals and that comorbidity is common (> 70% have concurrent conditions).

Many risk factors were found to affect the emergence of ASD, which most often occur together. The most common factors that can lead to ASD include: cesarean section, prenatal complications (antepartum hemorrhage, diabetes, preeclampsia, stress, subchorionic hematoma, hydronephrosis, low umbilical cord blood flow, infection, prolonged leakage of amniotic fluid after amniocentesis), medications during pregnancy, infections, diseases or injuries in the first years of a child's life, vaccine, febrile condition, maternal illnesses/infections during pregnancy, maternal age > 35 years, perinatal complications (premature delivery, oligohydramnios, breech fetal position, post-term pregnancy, asphyxia, placental abruption, failure to progress, previous miscarriage, low birth weight, incubator/oxygen, history of genetic diseases, and paternal illnesses. Mothers often say that pregnancy with a child with ASD was more difficult.

Several prenatal factors in our research, such as parents over 35 years of age, parents' race, and maternal diseases during pregnancy, are associated with one meta-analysis (Wang et al., 2017). Similarities between the two studies were found in the following perinatal factors: cesarean section, prematurity, spontaneous delivery, induced delivery, breech fetal position, preeclampsia, and fetal distress. Furthermore, postnatal factors associated with the increased risk of ASD were brain anomaly, low birth weight, postnatal bleeding, and male gender (Wang et al., 2017).

Although in each child the symptoms vary, parents, special educators and rehabilitators, and the professional team reported the following as the most common symptoms: absence of speech, delayed or inappropriate speech with regard to age, not responding to their name, no eye contact, poor social skills, hyper/hyposensitivity, and isolation. Our results are in accordance with the research by Parmeggiani et al. (2019), where they conclude that social interaction and relationships (93.3%) and language (92.4%) are the categories of early signs represented the most in their sample.

Our results show that ASD most often occurs isolated. However, when accompanied by other conditions, the most common comorbidities were: epilepsy, ADD, CP, ID, and delayed psychomotor development. Trajkovski (2019) found that persons with ASD had high frequencies of one or more co-occurring non-ASD developmental, psychiatric, neurologic, metabolic, immune, gastrointestinal, and possibly causative medical diagnoses. Medical co-morbidity and consecutive pathological processes can negatively affect the behavior, socialization, communication, cognitive function, and sensory processing of individuals with autism (Trajkovski, 2019).

According to the results, the most frequently used diagnostic tests and methods are M-CHAT, anamnesis, observation, and neurological examination. However, the drawback is that around 17% do not use any diagnostic tests or methods for detecting ASD.

At present, ASD can be diagnosed with a high degree of reliability between 18 months and 2 years of age. However, the first symptoms are already present long before the diagnosis is made (Paula-Pérez & Artigas-Pallarés, 2014). In our study, the symptoms of ASD were noticed even at six months of age, but the mean age of the onset of the symptoms was 2.2 years, indicating the aim of diagnosing ASD as soon as possible.

The mean age of diagnosis used to be 5.6 years, while it has been 4.2 years in the past 10 years. This shows that ASD diagnosis has been obtained earlier in the last 10 years, which means the diagnostic methods and practices have improved. Some authors report the global average age of ASD diagnosis as determined by the meta-analysis based on 35 studies from 35 countries, comprising 66,966 individuals with ASD. The current mean age of ASD diagnosis is 60.48 months (95% *CI*: 50.12–70.83) with a range of 30.90–234.57 months. Although progress is being made, early detection of ASD should continue to be a global priority (Van't Hof et al., 2020).

Over the years, there has been an improvement in the age reduction of diagnosis to 1.4 years, while the waiting time from noticing the first symptoms until obtaining the ASD diagnosis is 2.1 years. However, this is still very different from the research conducted by Penner et al. (2018), where the results show that the average waiting time for diagnosis is 7 months.

There is also a large number of children (one-third) with misdiagnosis, which as a value is greater than the results obtained by King & Bearman (2009), where changes in practices for diagnosing ASD had a significant effect on the number of ASD cases, which is a quarter of the increase in California prevalence between 1992 and 2005.

Recommendations

From the results of this research, and the conclusions we can make, the following recommendations may be welcome for future practice: using M-CHAT as a diagnostic tool that helps in making a diagnosis, greater use of ADI-R, ADOS, and DSM-5 criteria. Apart from the formal diagnostic process, informing all professionals working with children about early ASD symptoms and how to recognize the condition is especially important. We should emphasize the significance of raising parents' awareness of the proper development, deviations from it, and how to recognize when they should contact a professional. Finally, everyone involved in the development of these children should focus on the latest research on etiology, children's monitoring approach, diagnostic procedures and tests, and conducting more research on this topic in our country.

Limitations

This research has some limitations, the first of which is the sample size. The impact of selection bias can be a result of sampling, nonresponse, and poor coverage of people with no internet. Due to the low response rate, the results could not be generalized beyond the sample. We had limited ability to gain access to the appropriate type or geographic scope of participants. Thus, the people who responded to our survey questions may not truly be a random sample. There is no specific information about the gender structure, age, years of work experience, and institutions in which the professionals work. We do not have information on the number of children with ASD that the parents have. Also, the experiences reported by parents versus professionals may not be directly comparable since professionals' perceptions were based on a large sample of experiences while users' perceptions were limited to their personal experiences.

Conclusions

ASD is more common in males in the ratio of 3:1. The most common factors that can lead to ASD are: cesarean section, prenatal complications (bleeding, diabetes), medications during pregnancy, infections, illnesses or injuries in the first years of a child's life, maternal illnesses/infections during pregnancy, mother age > 35y, perinatal complications (premature delivery, oligohydramnios) miscarriage, and low birth weight.

Each child's symptoms are different, but the most common symptoms, regardless of age, include: lack of speech, delayed or inadequate speech for a specific age, not responding to their name, no eye contact, weak social skills, hyper/hyposensitivity, and isolation.

The prevalence of ASD as an isolated case is higher, and if it is accompanied by comorbid disorders, they most often include: epilepsy, ADD, CP, ID, and delayed psychomotor development.

The most commonly used diagnostic tests and procedures for diagnosing ASD are: M-CHAT, anamnesis, and observation.

There is a significant difference in the claims about the age at which the ASD diagnosis is obtained. On the one hand, professionals say the mean age is 3.5 years, while according to the parents, it is 4.5 years. The age of diagnosis used to be 5.6 years, while it has been 4.2 years in the past 10 years.

The waiting time frame from noticing the first symptoms to getting the ASD diagnosis is 2.1 years. Compared to before, the number of institutions visited by parents before receiving a definite diagnosis of ASD is lower. More than a third of the children are misdiagnosed. The most common misdiagnoses are: developmental dysphasia, alalia, and disharmonious development. The obtained results refer to the sample of this research and thus cannot be applied to the general population of children with ASD in Macedonia.

Children with ASD have an increased need for pediatric and psychiatric specialist services, both for their core functional deficits and concurrent medical conditions. Appropriate and individualized medical assessment must be carried out in all cases, including a documented clinical examination.

Acknowledgements

Special thanks to all the participants in this research study and their willingness to share their personal experience. The authors are also grateful to colleague Marina Antonijević from Special Primary School "Miloje Pavlović" in Belgrade for proofreading the abstract in the Serbian language.

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Važnost rane dijagnoze kod poremećaja iz spektra autizma za adekvatan tretman i rehabilitaciju u Makedoniji

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Uvod: Poremećaj iz spektra autizma (PSA) ima nejasnu etiologiju i nije poznat univerzalni tretman, što otežava dobijanje tačne i blagovremene dijagnoze. Broj dokaza koji ukazuju na važnost rane dijagnoze i tretmana raste. *Cilj*: Istraživanje je urađeno da bi se procenio uticaj rane dijagnoze i njen značaj, kao i efikasnost u postavljanju dijagnoze u proteklim godinama i decenijama u Makedoniji. *Metodologija*: Izvršili smo uporednu analizu prikupljenih podataka od 95 ispitanika podeljenih u tri grupe, od kojih su 30 roditelji, 35 su specijalni edukatori i rehabilitori, a 30 članovi profesionalnog tima koji učestvuju u dijagnostikovanju autizma. Korišćen je originalni istraživački instrument u obliku tri upitnika. *Rezultati*: Mnogi prenatalni, perinatalni i postnatalni faktori mogu dovesti do PSA. Najčešći simptomi su: nedostatak govora, kašnjenje u razvoju govora, neodazivanje na ime, izostanak kontakta očima, nedovoljno razvijene socijalne veštine, hiper/hiposenzibilnost, izolacija. Autizam se češće javlja kao primarni, nego sekundarni. Srednja vrednost uzrasta na kome se postavlja dijagnoza ranije je bila 5.6 godina a u poslednje vreme je 4.2 godine. Na postavljanje dijagnoze čeka se oko 2.1 godinu od prvih primećenih simptoma. Roditelji posećuju manje institucija u procesu dobijanja dijagnoze. Još uvek postoji značajan broj pogrešno uspostavljenih dijagnoza. *Zaključak*: Mnogi faktori igraju ulogu u pojavi autizma. Postoje određeni simptomi koji se pojavljuju u većini slučajeva. U poslednjoj deceniji dijagnoza autizma se uspostavlja na ranijem uzrastu. Poboljšan je pristup i proces dijagnostikovanja autizma.

Ključne reči: poremećaji iz spektra autizma, rana dijagnoza, tretman, rehabilitacija

PRIMLJENO: 10.03.2022.
REVIDIRANO: 31.05.2022.
PRIHVAĆENO: 15.06.2022.