

PHYSICAL COMORBIDITIES IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

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ABSTRAK

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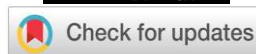
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Abstract:

Autism Spectrum Disorders (ASD) is a neurodevelopmental disorder characterized by two core symptoms; impairments in social communication and restricted or repetitive behavior. ASD is a broad group of conditions where patients have a variety of abilities and needs. Their ASD related-physical and psychological comorbidities also affect their mortality risk. This study wished to investigate physical comorbidities associated with ASD in the national reference hospital in Indonesia. This is a descriptive study with a cross-sectional approach on children with ASD who visited RSUP Dr. Mohammad Hoesin, Palembang, during 2014-2018. Data were obtained from the medical records and telephone interviews with the parents. Of all the 60 participants included in the study, most are male (n=52;86,7%). The most prevalent ASD-related physical comorbidities were gastrointestinal disorders (n=27;45%), followed by nervous system disorders (n=35;58,3%), and immune system disorders (n=11;18,3%). Despite the small sample size, the prevalence of ASD-related physical comorbidities in children with ASD is profoundly high, implying the need to do early detection from both parents and health professionals to prevent morbidity and complications that may occur. Children with autism can benefit from various therapies start in early childhood and continue throughout their lives to improve their development, and quality of life.

Abstrak:

Autism Spectrum Disorders (ASD) adalah gangguan perkembangan saraf yang ditandai dengan dua gejala inti; gangguan dalam komunikasi sosial disertai perilaku terbatas atau berulang. Komorbiditas fisik dan psikologis terkait ASD yang dialami oleh pasien dapat mempengaruhi risiko mortalitas. Penelitian deskriptif observasional ini bertujuan untuk mengetahui komorbiditas fisik yang berhubungan dengan ASD di RSUP Dr. Mohammad Hoesin, Palembang, selama tahun 2014-2018. Data diperoleh dari rekam medis dan wawancara telepon dengan orang tua pasien. Dari total 60 sampel yang termasuk dalam penelitian ini, sebagian besar adalah laki-laki (n=52;86,7%). Komorbiditas fisik terkait ASD yang paling umum adalah gangguan gastrointestinal (n=27;45%), diikuti oleh gangguan sistem saraf (n=35;58,3%), dan gangguan sistem imun (n=11;18,3%). Meskipun ukuran sampel relative kecil, prevalensi komorbiditas fisik terkait ASD pada anak-anak dengan ASD sangat tinggi, menyiratkan perlunya deteksi dini dari orang tua dan tenaga kesehatan untuk mencegah morbiditas dan komplikasi yang mungkin terjadi. Anak-anak dengan autisme dapat memperoleh manfaat dari berbagai terapi yang dimulai pada masa kanak-kanak dan berlanjut sepanjang hidup mereka untuk meningkatkan perkembangan, dan kualitas hidup mereka.



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INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by two core symptoms, impairments in social communication and restricted or repetitive behavior[1]. Comorbidities that accompany ASD are often undiagnosed because of the atypical symptoms of the disease. Individuals with ASD with nonverbal or minimal verbal ability cannot verbally express their pain or discomfort and tend to demonstrate it through disruptive behaviors, including aggression and self-injury[2]. The most common GI symptoms are flatulence, bloating, abdominal pain, diarrhea, belching, gastroesophageal reflux, and constipation[3]. The estimated prevalence of GI problems in children with ASD varied between 9 to 70%[4]. Gastrointestinal comorbidities are related to a higher degree of irritability, hyperactivity, anxiety, aggression, self-injury, and sleep disturbance[5] [6] [7]. Several pathophysiologies linked gastrointestinal symptoms and ASD. They include abnormal immune system function, increased intestinal permeability, dysbiosis of GI microbiota, and deficiency of various digestive enzymes[3] [7] [8] [9] [10].

Several studies suggest that comorbidities mediated by the immune system occur in children with ASD, such as asthma, allergic rhinitis, food allergies, and atopic dermatitis[11] [12]. The association between ASD and immune system disorders is, it has a similar cause, immune dysregulation. Clinical symptoms of asthma, food allergies, primary immunodeficiency, and other atopic diseases in children with ASD can increase the frequency of infections, symptoms of worsening behavior, and loss or decrease of acquired developmental and social skills[13]. Allergies can cause sleep disorders and hyperactivity. Pain and discomfort caused by allergies can also worsen the symptoms of ASD[14]. The comorbidity of nervous system disorders that most often occurs in individuals with ASD is epilepsy[15]. Other nervous system

disorders comorbidities are motor disorders, including difficulty in motor coordination, abnormal gait, postural control difficulties, and delayed learning of complex motor skills[16] [17] [18] [19].

RESEARCH METHOD

Patients who came into the growth and development children polyclinic in Dr. Mohammad Hoesin National Reference Hospital, Palembang and were later diagnosed with ASD based on DSM-IV a pediatrician consultant in child growth and development during the year 2020 were included in the study. Investigation through medical records provided the demographic data and the diagnosis along with physical comorbidities diagnosis, proceed with a telephone interview with the parents to gain some history and additional data. The age selection is ranging from 18 months to 18 years old. The data in this study were processed using the IBM SPSS 25 program to determine the frequency of the variables studied.

RESULTS AND ANALYSIS

This study obtained demographic characteristics including age, sex, nutritional status, and immunization status (table 1). From 360 patients diagnosed with ASD, 60 patients met the inclusion criteria. Based on age category, the most common age category was preschool (3–6 years old) with the prevalence of 75% (45 samples), with the mean age $4,01 \pm 1,98$ years old (2,03–5,99 years old) and the minimum age of one-year-old. The highest distribution of ASD patients based on sex was male, with a prevalence of 86,7% (n=52). Based on the vaccination status, most ASD patients received complete vaccination (68,3%, n=41). Nutritional status in ASD patients was good (55%, n=33).

From 60 samples, there were 57 (95%) ASD patients who experienced physical comorbidity. Each patient could experience either one, two, or three comorbidities at once. Physical comorbid-

ities found include gastrointestinal (GI) disorders (45%, n=27), nervous system disorders (58,3%,n=35), and immune system disorders in (18.3%, n=11). Table 2 shows the distribution and frequency of physical comorbidities that occurred in ASD patients.

Table 1.
The Distribution and Frequency of Demographic Characteristics of ASD Patients (n=60)

Demographic Characteristics	n	%
Age		
> 1 yo - ≤ 2 yo (late-infancy)	6	10
> 2 yo - ≤ 6 yo (early-childhood)	45	75
> 6 yo - ≤ 12 yo (late-childhood)	9	15
> 12 yo - ≤ 15 yo (pre-puberty)	0	0
> 15 yo - ≤ 18 yo (adolescents)	0	0
Sex		
Male	52	86,7
Female	8	13,3
Total	60	100

Table 2.
The Distribution and Frequency of Physical Comorbidities Occurred

Physical comorbidities	n	%
Gastrointestinal Disorders		
Diarrhea	22	36,7
Constipation	6	10
Nervous System Disorders		
Seizure	33	55
Epilepsy	5	8,3
Motor impairments (postural control difficulty, motoric coordination difficulties, abnormal gait, and motoric developmental delay)	3	5,0
Immune System		
Asthma	0	0
Atopic Dermatitis	2	3,3
Allergic Rhinitis	3	5,0
Food Allergic	7	11,7

As many as 22 patients with GI disorders experienced diarrhea (36,7%), and six experienced constipation (10%) (Table 2). Among those with nervous system comorbidities, 55% (n=33) had seizures, 8,3% (n=5) had epilepsy, and 5% (n=3) had motor impairments (Table 2). When it comes to immune system comorbidities, none experienced asthma, while few experienced atopic dermatitis (3,3%, n=2 samples), allergic rhinitis (5%, n=3), and food allergies (11,7%, n=7) as seen in Table 2.

DISCUSSION

Based on age category, the most common age category was preschool (3–6 years old) with the prevalence of 75% (45 samples), with the mean age 4,01±1,98 years old (2,03–5,99 years old) and the minimum age of one-year-old. However, a study conducted by Aldinger et al showed that the average age of ASD patients was 9.3 years old[20], which is inconsistent with the result of this study. This inconsistency might occur due to differences in the age characteristics of the samples. The highest distribution of ASD patients based on sex was male with a prevalence of 86,7% (52 samples). A systematic review study by Charman et al showed similar results, which stated ASD was diagnosed more frequently in boys than girls with a male: female ratio of 4:1[21]. This study is also following the results of the study by Aldinger et al which stated that the prevalence of ASD was dominated by males, with a prevalence of 78,3% [20].

The etiology and mechanisms underlying the prevalence of ASD in boys are higher than girls remain unknown. A study conducted by Ferri et al stated that fetal testosterone plays a role in various aspects of development and may interact with neuropeptides, neurotransmitters, and immune pathways, thus contributing to male susceptibility to neurodevelopmental

disorders, including ASD. Another hypothesis is that females are more sensitive to genetic disruptions, so they were unlikely to survive to term[22].

The prevalence of ASD patients who received complete vaccination was 68,3% (41 samples). What is considered to have a complete vaccination is if the patients have received a basic vaccination based on the Indonesian Department of Health recommendation. This result is aligned with the study by Goin et al which stated that the ratio of children with ASD who received DPT/DTaP, HepB, Hib, MMR, and polio are as high as 90%[23]. Nutritional status in ASD patients was found to be good with a prevalence of 55%. Research by Sharp et al showed similar results which showed that most children with ASD have a normal nutritional status, which was shown by a normal BMI to age with the prevalence of 68,6%[24].

From 60 samples, there were 57 (95%) ASD patients who experienced physical comorbidity. Similar results were shown by the study by Muskens et al which stated that the prevalence of physical comorbidities in ASD patients varied between 10,7 to 77,4%[25]. The result of this study shows that the prevalence of gastrointestinal disorders as ASD comorbidity is 45%. This result matched with the study conducted by Wasilewka and Kluwoski which stated the prevalence of gastrointestinal disorders in children with ASD varied between 9% to 84%.[3] The high prevalence of gastrointestinal disorders in children with ASD may occur due to the similar pathophysiological mechanisms underlying ASD and gastrointestinal disorders including abnormal immune system function, increased intestinal permeability, dysbiosis of digestive tract microbiota, and deficiency of various digestive enzymes[3] [7] [8] [26].

From all samples, it was found that the prevalence of diarrhea was 36,7%. This result is consistent with the study from Holingue et al which stated that the incidence of diarrhea in children with ASD

varied between 2,3% to 75,6%[27]. The prevalence of constipation in this study was 10%. This result is in line with the study conducted by Holingue et al which stated that the incidence of constipation in children with ASD varied between 4,3 to 45,5%[27].

The result of this study shows that the prevalence of seizures was 55% and the prevalence of epilepsy was 8,3%. This result is in line with research by Pacheva et al which stated that the prevalence of epilepsy as a comorbidity in ASD varied between 5% to 46%[28]. Until now, the prevalence of seizures in children with ASD remains unstudied, although there have been several studies that showed the correlation between seizures and ASD, and in theoretical discussion, a seizure is one of the physical comorbidities that shared similar pathophysiology to epilepsy. Seizure and/or epilepsy are comorbidities in ASD shown by the same pathogenesis i.e cortical development malformation[29].

The prevalence of ASD patients who experienced motor disorders was 5%. This result is inconsistent with the result of a systematic review by Moraes et al which stated the high prevalence of motor disorders in children with ASD, while the results of this study indicate that not many ASD patients at Mohammad Hoesin General Hospital experience motor disorders. This inconsistency may occur due to differences in the age of the samples in both studies. In a systematic review conducted by Moraes et al, the age of the sample obtained from the articles was 7 to 23 years old, whereas in this study the age of the samples was 1 to \leq 18-year-old, and no sample was found above the age of 10 years. The correlation between motor disorders and ASD is shown by the same pathogenesis i.e abnormalities in cerebellar development[19].

From all samples, the prevalence of immune system disorders is 18.3%. This result is not in line with the result of the study from Mostafa et al which stated the prevalence of allergic manifestation

(asthma, atopic dermatitis, allergic rhinitis, and food allergies) was 52%[30]. This incoherency may occur due to the different instruments used in diagnosing these comorbidities. In this study, the diagnosis of asthma, atopic dermatitis, allergic rhinitis, and food allergies was determined based on medical record data and telephone interviews with parents or caregivers of the patients, while the study by Mustofa et al, in addition to conducting anamnesis, the study also carried out physical examinations and other laboratory tests such as measuring serum Ig-E levels and peak expiratory flow rate using a Mini-Wright Peak Flow Meter[30].

The result of this study shows there were no ASD patients who experienced asthma. This result is consistent with the meta-analysis study conducted by Zheng et al which stated there was no correlation between asthma and ASD[31]. However, this result is inconsistent with the study from Kotey et al which stated children with ASD are more common to have asthma than normal development children, with the prevalence of 35%[32]. This inconsistency in prevalence may occur as a result of the difference in the number of samples in this study, which was 60 samples, which were lower compared to a study conducted by Kotey et al.

The result on the prevalence of food allergies was 11,7%. This result is aligned with the study from Gurney et al which stated the prevalence of food allergies in children with ASD was 14,1%[33]. The correlation between food allergies and ASD is shown by the same pathophysiology which is dysregulation of the immune system[12]. However, the study conducted by Akpınar et al shows inconsistent results, stating that the prevalence of food allergies in children with ASD was 8,4%. The study by Apkinar et al stated that there is no difference in the frequency of food allergies between children with ASD (8,4%) and children with normal development (8%). This inconsistency may be caused by the difference in place and

method used for collecting the data. In the study by Apkinar et al, the method for diagnosing food allergies was carried out by distributing questionnaires to parents of children with ASD conducted in school of special needs[34], whereas in this study the method used for diagnosing food allergies was based on medical record data at the hospital and interview with the patients' parents or caregiver using clinical criteria for food allergies.

From all samples, it was found that the prevalence of atopic dermatitis was 3,3%. These results are not in line with a study by Billeci et al which stated that children with ASD are more likely to have atopic dermatitis than children with normal development, with the prevalence that varied between 7% to 64,2%[13]. The inconsistency of this result may occur because, in this study, a history of atopic dermatitis was obtained through interviews with parents or caregivers of children with ASD based on clinical criteria of atopic dermatitis. Moreover, in this study, not all of the medical records contained the data of Ig-E levels, while in the comparative study, examination of Ig-E levels and other biomarkers were carried out. Increased serum Ig-E levels underlie atopic dermatitis as a comorbidity in ASD[12] [35].

From all samples, it was found that the prevalence of allergic rhinitis was 5%. This result is not consistent with the result of the study by Xu et al which stated that children with ASD are more often experienced allergic rhinitis with the prevalence of 18,73%[36]. This inconsistency may occur due to the large difference in sample number, where the study by Xu et al used more samples. Increased serum Ig-E levels underlie atopic dermatitis as a comorbidity in ASD[12] [35].

CONCLUSION

Based on the results of this study, it can be concluded that the prevalence of physical comorbidities in ASD pediatric patients in Mohammad Hoesin General

Hospital was high. The most common age category is preschool (3–6 years old), most of the patients were boys, with a good nutritional status, and received complete vaccination. The types of physical comorbidities found in patients were nervous system disorders, gastrointestinal disorders, and immune system disorders. The prevalence of ASD patients who experienced physical comorbidity is quite high implying attention from parents and health professionals is needed so that early detection can be done to prevent morbidity and complications that can occur.

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