

- Management of psychotropic medication side effects in children and adolescents. **Child and adolescent psychiatric clinics of North America**, 21(4), 713- 738.
17. Gardner, D. M., Baldessarini, R. J.& Waraich, P. (2005). Modern antipsychotic drugs: a critical overview. **Cmaj**, 172(13), 1703- 1711.
  18. Gerbers, J and A. J. Allen. (2005). "Atomoxetine in the treatment of patients with ADHD." **American Family Physician** 71(10): 1879.
  19. Ghandour, R. M., Sherman, L. J., Vladutiu, C. J., Ali, M. M., Lynch, S. E., Bitsko, R. H.& Blumberg, S. J. (2019). Prevalence and treatment of depression, anxiety, and conduct problems in US children. **The Journal of pediatrics**, 206, 256- 267.
  20. Horacek, J., et.al. (2006). "Mechanism of action of atypical antipsychotic drugs and the neurobiology of schizophrenia." **CNS drugs** 20(5): 389- 409.
  21. Jackson B and Lurie S. (2006). Adolescent depression: challenges and opportunities: a review and current recommendations for clinical practice. **Adv Pediatr**; 53: pp. 111- 163.
  22. Kris- Etherton PM, Harris WS, Appel LJ for the American Heart Association Nutrition Committee. (2003). Fish consumption, fish oil, omega- 3 fatty acids, and cardiovascular disease. *Circulation* 2002; 106:2747- 57. Erratum published: **Circulation**; 107:512.
  23. Lieberman JA, Stroup TS, McEvoy JP, et.al. (2005). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. **N Engl J Med**; 353:1209- 23.
  24. Lorberg, B., Davico, C., Martsenkovskiy, D.& Vitiello, B. (2019). **Principles in using psychotropic medication in children and adolescents. IACAPAP e- Textbook of Child and Adolescent Mental Health.** International Association for Child and Adolescent Psychiatry and Allied Professions.
  25. Luby, J., Mrakotsky, C., Stalets, M. M., Belden, A., Heffelfinger, A., Williams, M.& Spitznagel, E. (2006). Risperidone in preschool children with autistic spectrum disorders: an investigation of safety and efficacy. **Journal of Child& Adolescent Psychopharmacology**, 16(5), 575- 587.
  26. Mechler, K., Banaschewski, T., Hohmann, S.& Häge, A. (2022). Evidence- based pharmacological treatment options for ADHD in children and adolescents. **Pharmacology& Therapeutics**, 230, 107940.
  27. Michelson, D., Allen et.al. (2002). "Once- daily atomoxetine treatment for children and adolescents with attention deficit hyperactivity disorder: a randomized, placebo- controlled study." **American Journal of Psychiatry** 159(11): 1896- 1901.
  28. O'Mary, H. L. and Z. Cui. (2022). **Injectable Formulations of Poorly Water- Soluble Drugs. Formulating Poorly Water- Soluble Drugs**, Springer: 217- 252.
  29. Pringsheim, T., et.al. (2019). "Practice guideline recommendations summary: treatment of tics in people with Tourette syndrome and chronic tic disorders." **Neurology** 92(19): 896- 906.
  30. Santosh, P.& Suren, R. (2008). Pediatric psychopharmacology- special considerations. **Psychiatry**, 7(9), 384- 388.
  31. Schneider, B. J., et.al. (2007). "Psychiatric medications for deployment: An update". **Military Medicine** 172(7): 681- 685.
  32. Sood, S., et.al. (2008). Priapism associated with atypical antipsychotic medications: a review. **International Clinical Psychopharmacology** 23(1): 9- 17.
  33. Spencer, T., et.al. (1998). "Effectiveness and tolerability of atomoxetine in adults with attention deficit hyperactivity disorder." **American Journal of Psychiatry** 155(5): 693- 695.
  34. Spriet S, and Banks TA. (2015). Drug reaction with eosinophilia and systemic symptoms syndrome. **Allergy Asthma Proc**; 36:501-5.
  35. Zwaigenbaum L et.al. (2015). Early screening of autism spectrum disorder: recommendations for practice and research. **Pediatrics**. 136(suppl 1): S41-59.

abdominal pain, epigastric pain in 16.7% i.e., 1 out of 6 of patients. Diarrhea in 50% i.e., 3 out of 5 of patients. Other side effects reported are fatigue, flu- like symptoms, headache in 16.7% i.e., 1 out of 6, as represented by table (1).

This is in line with previous studies as; common dose- dependent side effects of fish oil, omega- 3 fatty acids include a fishy aftertaste (dysgeusia), GIT disturbances 4.9%, and nausea 1.4%. (Kris- Etherton et.al, 2003)

In the present study, citicoline reported with minimum adverse effects. This is in consistent with previous studies of citicoline in children, with minimal occurrence of adverse events, confirm its high level of safety. (Fresina et.al, 2008)

#### **Conclusions, Recommendations, and Clinical Significances:**

Pharmacovigilance of psychotropic drugs is a vital process to inform clinicians with the most recent reports of side effects, so it is important to stabilize the process of pharmacovigilance in integrated management of children with disabilities. Prescribing psychotropic drugs is a difficult process due to side effects; so that, it is essential for prescribers to know the formula for calculation of the doses of psychotropic drugs; initial, target, maximum doses, also, it is essential to consider drug interactions of psychotropic drugs.

Treatment with psychotropic drugs in children and adolescents needs continuous monitoring for adverse drug reactions. It is recommended to continuously reassess the need for continuous treatment with psychotropic drugs. Follow up of patients during therapy with psychotropic drugs is essential to continuously check for the emergence of new side effects and to mitigate or relieve these side effects. Regular laboratory monitoring of the complete blood count, blood glucose level, lipid profile before and during therapy with psychotropic drugs, and repeated measurement of anthropometric measures e.g., body weight is recommended.

Because of the limited sample size in this study, further studies are needed to confirm these results. Larger studies to report adverse drugs reactions are needed in greater detail and to search for new methods for reporting, prediction, and early detection of side effects of psychotropics to either prevent or treat them.

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#### **References:**

1. AAP. (2022). **American Academy of Pediatrics: Initial Medical Evaluation of a Child Diagnosed with an Autism Spectrum Disorder**. AAP website. Accessed September 22, 2022. [https://www.aap.org/enus/Documents/cocd\\_fact\\_sheet\\_initialmedicine.pdf](https://www.aap.org/enus/Documents/cocd_fact_sheet_initialmedicine.pdf).
2. APA. (2022). American Psychiatric Association: Autism spectrum disorders. In: **Diagnostic and Statistical Manual of Mental**

**Disorders**. 5<sup>th</sup> ed. Text Revision. American Psychiatric Association; 2022:57- 69.

3. Abdulrasool, Z. (2022). The development of a pharmacovigilance system in Bahrain. **Saudi Pharmaceutical Journal**, 30(6), 825- 841.
4. Atabay, E.& Arman, A. R. (2019). 11<sup>th</sup> International Congress on Psychopharmacology& 7<sup>th</sup> International Symposium on Child and Adolescent Psychopharmacology. **Psychiatry**, 29(S1), 129- 263.
5. Bitsko, R. H., Holbrook, J. R., Ghandour, R. M., Blumberg, S. J., Visser, S. N., Perou, R.,& Walkup, J. T. (2018). Epidemiology and impact of health care provider- diagnosed anxiety and depression among US children. **Journal of developmental and behavioral pediatrics: JDBP**, 39(5), 395.
6. Blier, P. and C. de Montigny. (1999). "Serotonin and drug- induced therapeutic responses in major depression, obsessive- compulsive and panic disorders." **Neuropsychopharmacology** 21(2): 91S- 98S.
7. Bostwick, J. R., et.al. (2009). "Antipsychotic-induced hyperprolactinemia." **Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy** 29(1): 64- 73.
8. Bymaster, F. P., et.al. (2002). "Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder". **Neuropsychopharmacology** 27(5): 699- 711.
9. Correll, C. U., et.al. (2021). Pharmacokinetic characteristics of long-acting injectable antipsychotics for schizophrenia: an overview. **CNS drugs** 35(1): 39- 59.
10. De Hert, M., Detraux, J., Van Winkel, R., Yu, W.& Correll, C. U. (2012). Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. **Nature Reviews Endocrinology**, 8(2), 114- 126.
11. Doghramji, K.& Jangro, W. C. (2016). Adverse effects of psychotropic medications on sleep. **Psychiatric Clinics**, 39(3), 487- 502.
12. Druschky, K., Toto, S., Bleich, S., Baumgärtner, J., Engel, R. R., Grohmann, R.& Degner, D. (2021). Severe drug- induced liver injury in patients under treatment with antipsychotic drugs: Data from the AMSP study. **The World Journal of Biological Psychiatry**, 22(5), 373- 386.
13. Fallah, M. S., Shaikh, M. R., Neupane, B., Rusiecki, D., Bennett, T. A.& Beyene, J. (2019). Atypical antipsychotics for irritability in pediatric autism: a systematic review and network meta- analysis. **Journal of Child and Adolescent Psychopharmacology**, 29(3), 168- 180.
14. Feduccia, A. A., Jerome et.al. (2019). "Breakthrough for trauma treatment: safety and efficacy of MDMA- assisted psychotherapy compared to paroxetine and sertraline". **Frontiers in psychiatry** 10: 650.
15. Fresina, M., et.al. (2008). "Effect of oral CDP- choline on visual function in young amblyopic patients". *Graefe's Archive for Clinical and Experimental Ophthalmology* 246(1): 143- 150.
16. Garcia, G., Logan, G. E.& Gonzalez- Heydrich, J. (2012).

with and without risk factors for seizures or preexisting seizure disorders during post- marketing use of the drug. Fatigue is more frequently occur in those receiving atomoxetine (6- 9% vs. 2- 4%). (Gerbers& Allen 2005)

In placebo- controlled clinical trials in pediatric patients: the reported CNS effects were drowsiness (11% vs. 4%) and dizziness (5% vs. 2%). Insomnia 0.9% and drowsiness 0.3% were among the main causes for the study discontinuation in pediatric patients. (Spencer et.al, 1998)

Fluoxetine was the first SSRI to be marketed in the U.S. Fluoxetine was the first SSRI to receive approval in pediatric patients 8 years and older with major depressive disorder and is the most extensively evaluated SSRI in pediatric depression. The drug is also indicated for pediatric patients 7 years and older for the treatment of OCD. Fluoxetine is a potent inhibitor of CYP2D6. All antidepressants contain a warning box related to an increased risk of suicidality in children, and adolescents during the initial therapy; so, it is essential to consider the potential risks in these age groups. (Schneider et.al, 2007)

In the present study, Fluoxetine side effects reported including rash in (20% i.e., 1 out of 5), GIT side effects reported in 100% i.e., 5 out of 5 as anorexia, nausea, vomiting, abdominal pain, epigastric pain, diarrhea (20% i.e., 1 out of 5), and constipation (20% i.e., 1 out of 5), jaundice in 20% i.e., 1 out of 5 of patients. CNS side effects reported as insomnia (40% i.e., 2 out of 5), agitation (100% i.e., 5 out of 5), aggression (80% i.e., 4 out of 5), weight loss (60% i.e., 3 out of 5) as represented in table (2).

These results are in line with previous reports of GIT side effects more frequently in those receiving fluoxetine than placebo: nausea (12% to 29%), diarrhea (8% to 18%), anorexia (4% to 17%), xerostomia (4% to 12%), dyspepsia (6% to 10%), constipation 5%, flatulence 3%, vomiting 3%, and weight loss 2%. Anorexia can result from serotonin- reuptake blockade, and tolerance to this effect does not appear to occur. In clinical practice, weight loss > 5% of body weight has been reported in 10% to 15% of fluoxetine- treated patients; weight loss corresponds to increasing dose. Periodically assess weight, especially in those who are underweight. Periodic monitoring of weight is recommended for all pediatric patients receiving fluoxetine. In addition, CNS side effects as insomnia (10% to 33%), anxiety (6% to 15%), nervousness (8% to 14%), drowsiness (5% to 17%), tremor (3% to 13%), abnormal dreams (1% to 5%), headache 21%, dizziness 9%. Agitation, and hyperkinesia were reported in pediatric patients receiving fluoxetine at an incidence of at least 2% and at a rate which was greater than placebo. Emotional lability, agitation, amnesia, confusion, and sleep disorder occurred in 1% or more of patients during premarketing evaluation. (Schneider et.al, 2007)

Sertraline is an oral SSRI; indicated for treating OCD in pediatric patients 6 years and older. Product labels for all antidepressants contain a boxed warning related to an increased risk of suicidality in children, adolescents, and young adults during the initial stages of therapy when treating depression or other conditions; therefore, the necessity of pharmacologic therapy versus the potential risks should be carefully considered in these populations (Feduccia et.al, 2019). SSRIs may act by

selective serotonin reuptake blockade at the neuronal membrane, which enhances the actions of serotonin. Initially, SSRIs increase availability of serotonin in the somatodendritic area through serotonin reuptake blockade at the serotonin transport pump. During long- term administration of SSRIs, serotonin autoreceptors are down- regulated and desensitized, allowing the neuron to increase serotonin release in the axon terminal synapses and increase its neuronal impulses. Because of the delay in therapeutic response to SSRIs, it is theorized that the change in the balance of serotonin receptors over time is an important mechanism of effect. (Blier & de Montigny, 1999)

In the present study, sertraline side effects reported including GIT side effects reported in as anorexia (100% i.e., 5 out of 5), nausea (80% i.e., 4 out of 5), vomiting (60% i.e., 3 out of 5), abdominal pain (20% i.e., 1 out of 5), epigastric pain (40% i.e., 2 out of 5), constipation (40% i.e., 2 out of 5), diarrhea in 60% i.e., 3 out of 5 of patients. CNS side effects reported as insomnia (60% i.e., 3 out of 5), agitation (60% i.e., 3 out of 5), aggression (20% i.e., 1 out of 5). Pallor (20% i.e., 1 out of 5), fatigue (60% i.e., 3 out of 5), flu- like symptoms (20% i.e., 1 out of 5), headache (80% i.e., 4 out of 5), as represented by table (2).

These reported side effects are matched with previous studies in pediatric clinical trials in at least 2% of pediatric patients and at a rate of at least twice the placebo rate include hyperkinesia. Other centrally mediated effects reported during premarketing evaluation and occurring in less than 2% of patients receiving sertraline included ataxia, coma, decreased alertness, hypoesthesia, syncope, lethargy, and psychomotor hyperactivity. During postmarketing use, extrapyramidal symptoms (i.e., akathisia, dystonic reaction including oculogyric crisis) have been reported. Adverse reactions were reported in at least 2% of pediatric patients and at least twice the rate of placebo included aggression and anxiety. Anti- depressants can precipitate mania in susceptible individuals. Sertraline should be introduced cautiously in patients with a seizure disorder and promptly discontinued if seizures develop. SSRIs such as sertraline, may cause hyponatremia, which is frequently the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). the adverse effect appeared reversible upon discontinuation of the causative SSRI. (Feduccia et.al, 2019)

During post- marketing use of fluoxetine or sertraline, the following adverse cutaneous drug reactions are reported; such as maculopapular rash or urticaria which disappear with treatment by anti- histaminic or corticosteroid, or upon discontinuation of the drug, but there are other severe, potentially fatal adverse cutaneous drug reactions reported such as angioedema, Steven- Johnson syndrome (SJS), and Toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS). Treatment should include stopping the offending drug quickly and initiating the appropriate medical treatment. (Spriet and Banks; 2015)

In the present study, omega- 3 fatty acids produce rash (16.7% i.e., 1 out of 6). GIT side effects reported are anorexia, nausea, vomiting,

stabilizers stimulants, and antipsychotics. (Garcia et.al, 2012)

Risperidone may act via central blockade of D-2 in the mesolimbic pathway. Antipsychotic drugs also have neuroplastic effects, such as synaptic plasticity (remodeling of synapses and development of new neuronal connections) and neurogenesis (development of new neurons), suggesting that it may take some time before some of the therapeutic effects appear. (Horacek et.al, 2006)

In the present study, the side effects reported with risperidone are unpalatable 80% i.e., 4 out of 5 of patients, skin rash in 20% i.e., 1 out of 5, GIT adverse effects including anorexia (20% i.e., 1/ 5), nausea (20% i.e., 1/ 5), vomiting (20% i.e., 1/ 5), abdominal pain (20% i.e., 1/ 5), epigastric pain (20% i.e., 1/ 5). CNS adverse effects including sedation (80% i.e., 4/ 5), sleepiness (80% i.e., 4/ 5), confusion (40% i.e., 2/ 5), tremors (20% i.e., 1/ 5), ataxia (60% i.e., 3/ 5), convulsions (20% i.e., 1/ 5). Other side effects including fatigue (20% i.e., 1/ 5), and weight gain (40% i.e., 2/ 5) as represented by table 1.

These results are in line with those reported in pediatric clinical trials as Gardner et.al, 2005; who reported GI side effects include hypersalivation (up to 10%), upper abdominal pain (13% to 16%), nausea (8% to 16%), vomiting (10% to 20%), diarrhea (7% to 8%), constipation 17%, dyspepsia (3% to 10%), xerostomia 10%, and epigastric discomfort (up to 6%).

CNS adverse effects; sedation or sleepiness (12% to 63%), fatigue (18% to 31%), drooling 12%, headache 12%, and dizziness (7% to 16%). Furthermore, in pediatric patients taking oral risperidone reported pseudo-parkinsonism (6% to 28%), tremor (8% to 11%), akathisia (0% to 10%), and dystonic reactions (2% to 6%). Akathisia may develop several days to weeks of therapy and may respond to reduction of dosage or concomitant administration of a benzodiazepine (e.g., lorazepam) or a beta-blocker (e.g., propranolol, metoprolol). (Lieberman et.al, 2005)

Metabolic changes including hyperglycemia, hyperlipidemia. Hyperglycemia and diabetes mellitus were reported in patients treated with atypical antipsychotics including risperidone. Hyperlipidemia, including hyper-cholesterolemia and hyper-triglyceridemia have been reported during post-marketing use of risperidone. Discontinuation of risperidone therapy should be considered if symptoms are severe. (De Hert et.al, 2012)

CBC including WBC count should be carefully monitored during the first few months of therapy with risperidone. Drug should be discontinued in case of significant decrease in WBC count. Risperidone should be discontinued if Absolute Neutrophil Count <1000/mm<sup>3</sup> and follow the WBC count until recovery (Atabay& Arman, 2019). Also, increase level of hepatic enzymes and gamma-glutamyl transferase have been reported. (Druschky et.al, 2021)

Aripiprazole is one of the atypical antipsychotic drugs, belongs to a class of medications called dopamine system stabilizers (DSSs). Contrast to all other antipsychotics, which are full dopamine antagonists, aripiprazole is a partial dopamine agonist. Aripiprazole used to treat

children 6 years of age and older with irritability associated to autism disorder or with tics related to Tourette's syndrome. Aripiprazole mitigates the severity of tics in patients with Tourette's syndrome or chronic tic disorders. (Pringsheim et.al, 2019)

In the present study, aripiprazole produces skin rash (80% i.e., 4 out of 5), GIT adverse effects including anorexia (100% i.e., 5 out of 5), nausea (80% i.e., 4 out of 5), vomiting (100% i.e., 5 out of 5), abdominal pain (80% i.e., 4 out of 5), epigastric pain (20% i.e., 1 out of 5). CNS adverse effects including sedation, sleepiness, and tremors (100% i.e., 5 out of 5), confusion (20% i.e., 1 out of 5), ataxia (60% i.e., 3 out of 5), convulsions (20% i.e., 1 out of 5). Other side effects including fatigue (100% i.e., 5 out of 5), flu-like symptoms (20% i.e., 1 out of 5), as represented by table (1).

This is in consistent with previous studies; in pediatric clinical trials; GI side effects that were reported more frequently with oral aripiprazole than with placebo; included nausea (8% to 11%), vomiting (8% to 14%), constipation 2%, diarrhea 4%, upper abdominal pain 3%, abdominal discomfort 2%, drooling (3% to 9%), loss of appetite (5% to 7%), and hypersalivation (4% to 6%). Fatigue and lethargy were reported in (8% to 17%) of patients, and headaches in 10% to 12%. (Correll et.al, 2021)

In clinical trials in pediatric patients treated by oral aripiprazole, somnolence; including sedation or drowsiness, was the most frequent adverse effect of aripiprazole reported in 4% to 23% of (O'Mary and Cui 2022).

Atomoxetine is a selective norepinephrine reuptake inhibitor (NRI) and was the first non-stimulant drug approved for ADHD (Gerbers& Allen; 2005). It is similar in structure to fluoxetine, does not have a potential for abuse, and is not classified as a controlled substance. Atomoxetine is safe and effective in adults and pediatric patients 6 years and older with ADHD with DSM-IV criteria (for inattentive subtype and both inattentive and hyperactive/impulsive subtypes) (Michelson et.al, 2002). It is theorized that the atomoxetine-induced increase in NE in the prefrontal cortex, a region involved in attention and memory, mediates the therapeutic effect of atomoxetine in ADHD. (Bymaster et.al, 2002)

In the present study, atomoxetine produces adverse effects include anorexia (100% i.e., 5 out of 5), nausea (60% i.e., 3 out of 5), abdominal pain (20% i.e., 1 out of 5), constipation (20% i.e., 1 out of 5), diarrhea (40% i.e., 2 out of 5), jaundice (20% i.e., 1 out of 5). CNS adverse effects include agitation (60% i.e., 3 out of 5), fatigue (40% i.e., 2 out of 5), headache (40% i.e., 2 out of 5), other side effects; bone aches (20% i.e., 1 out of 5), weight loss (20% i.e., 1 out 5); as represented in table (2).

These results are in line with previous studies; placebo-controlled clinical trials in pediatric patients, weight loss (3% vs 0%), decreased appetite (16% vs 3%), and anorexia (3% vs 1%) occurred more frequently with atomoxetine than placebo. Discontinue atomoxetine in any patient who exhibits jaundice or laboratory evidence of liver injury. Atomoxetine should not be restarted in these patients. Neurologic side effects including seizures occurred in 0.2% of pediatrics, in clinical trials that followed premarket testing of atomoxetine. Seizures have been reported in those

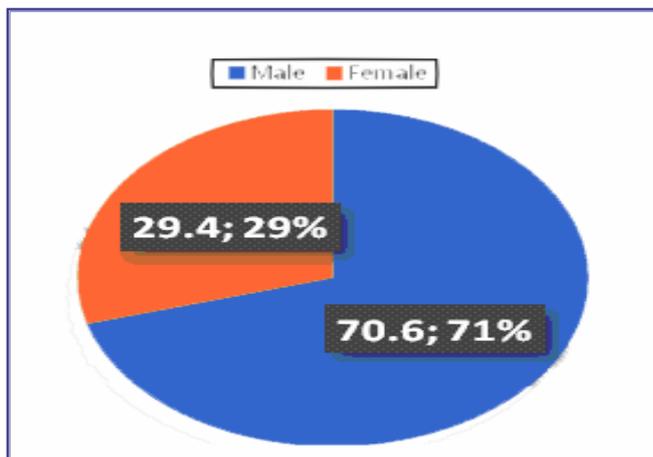


Fig. (1) Gender distribution of studied patients.

In this study, males represented about 71%, while female represented 29%, which consistent with the high prevalence of psychiatric disorders as ASD, ADHD in boys than girls.

Patients were diagnosed with psychiatric disorders according to DSM-5; which were collected as follow; ASD (38.2% i.e., 13 out of 34); ADHD (29.4% i.e., 10 out of 34); Depression (8.8% i.e., 3 out of 34), OCD (5.9% i.e., 2 out of 34); Dyslexia (5.9% i.e., 2 out of 34); ODD (2.9% i.e., 1 out of 34); PTSD (2.9% i.e., 1 out of 34); GAD (2.9% i.e., 1 out of 34); and ID (5.9% i.e., 1 out of 34), as shown in Fig. (2).

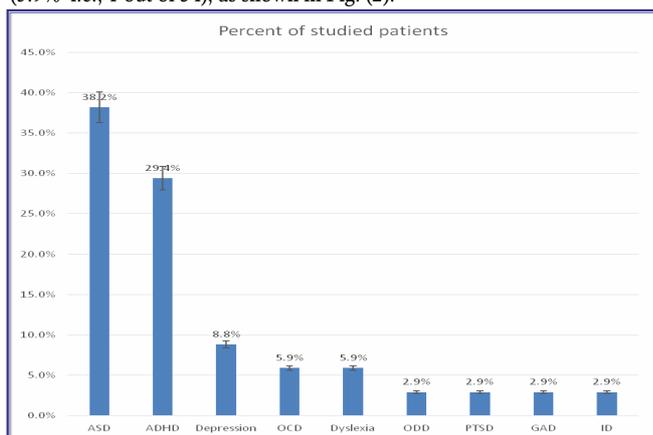


Figure (2) The Percentages of diagnoses of the studied patients.

In this study patients diagnosed with ASD, ADHD and depression are the most common, which indicates the high prevalence of these disorders among children with disabilities.

Table (1) Side effects reported during therapy with anti- psychotic drugs; risperidone and aripiprazole, and omega- 3 FAs

Side Effects	Risperidone (n= 5)		Aripiprazole (n= 5)		Omega-3 FA (n= 6)	
	n	%	n	%	n	%
Un- Palatable	4	80	0	-	4	66.7
Skin Rash	1	20	4	80	1	16.7
Anorexia	1	20	5	100	1	16.7
Nausea	1	20	4	80	1	16.7
Vomiting	1	20	5	100	1	16.7
Diarrhea	-	-	-	-	3	50
Abdominal Pain	1	20	4	80	1	16.7
Epigastric Pain	1	20	1	20	1	16.7
Sedation	4	80	5	100	-	-
Sleepiness	4	80	5	100	-	-
Confusion	2	40	1	20	-	-
Agitation	1	20	-	-	-	-
Tremors	1	20	-5	100	-	-

Side Effects	Risperidone (n= 5)		Aripiprazole (n= 5)		Omega-3 FA (n= 6)	
	n	%	n	%	n	%
Ataxia	3	60	3	60	-	-
Convulsions	1	20	1	20	-	-
Fatigue	1	20	5	100	1	16.7
Weight Gain	2	40	-	-	-	-
Flu- Like Symptoms	-	-	1	20	1	16.7
Headache	-	-	-	-	1	16.7

The most common side effects reported with risperidone are unpalatable, sedation, sleepiness, ataxia, weight gain.

The most common side effects reported with aripiprazole are anorexia, vomiting, sedation, sleepiness, tremors, fatigue.

The most common side effects reported with omega- 3 fatty acids are unpalatable, fishy odor, diarrhea.

Table (2) Side effects reported during therapy with non- stimulant and anti- depressant drugs, fluoxetine and sertraline

Side Effects	Atomoxetine (n= 5)		Fluoxetine (n= 5)		Sertraline (n= 5)	
	n	%	n	%	n	%
Un- Palatable	-	-	-	-	-	-
Skin Rash	-	-	1	20	-	-
Anorexia	5	100	5	100	5	100
Nausea	3	60	5	100	4	80
Vomiting	-	-	5	100	3	60
Diarrhea	2	40	1	20	3	60
Abdominal Pain	1	20	5	100	1	20
Epigastric Pain	-	-	5	100	2	40
Jaundice	1	20	1	20	-	-
Insomnia	-	-	2	40	3	60
Agitation	3	60	5	100	3	60
Aggression	-	-	4	80	1	20
Fatigue	2	40	-	-	3	60
Weight Loss	1	20	3	60	-	-
Flu- Like Symptoms	1	20	2	40	1	20
Headache	2	40	-	-	4	80
Palpitation	1	20	-	-	-	-

The most common side effects reported with atomoxetine are anorexia, nausea, diarrhea, agitation, headache, palpitation, weight loss.

The most common side effects reported with fluoxetine are anorexia, nausea, vomiting, insomnia, agitation, weight loss.

The most common side effects reported with sertraline are anorexia, nausea, vomiting, agitation, headache.

N.B; Minimal reported side effects reported with Citicoline.

**Discussion:**

Side effects due to psychopharmacologic treatment in children and adolescents range from the common adverse symptoms of headache, GIT distress, weight changes, and sleep disturbances to the more rarely reported but serious adverse cardiovascular, suicidal, and hypersensitivity events. Frequent monitoring and assessment of children and adolescents using standardized screening measures should occur in the context of increased risk for suicidality with antidepressants and antiepileptic drugs. Over the past 20 years there has been an increase in the use of psychotropic medication in children in the US. Unfortunately, there are few prospective double- blind placebo- controlled trials in children to guide clinicians in the safety and management of antidepressants, mood

**Introduction:**

Pharmacovigilance is the process of detection, assessment, understanding and prevention of adverse effects or any other drug-related problems to improve patient safety (Abdulrasul, 2022). Pediatrics pharmacovigilance for psychotropic drugs and long-term studies on efficacy and adverse effects are essential (Santosh& Suren, 2008). Pediatric psychopharmacology continues to develop rapidly, and clinicians must remain informed as new data about adverse effects of psychotropic drugs become available. (Lorberg et.al, 2019)

ASD is an early-onset neurodevelopmental disorder characterized by impairment in social communication and social interaction accompanied by restricted and repetitive behaviors, language delay and deficits in social skills are often noticed at age of 1 year; abnormal and repetitive behaviors often become obvious during the 2<sup>nd</sup> year of life (Zwaigenbaum et.al, 2015). No biomarker is available to confirm diagnosis; diagnosis is based on DSM-5- diagnostic criteria; confirmation requires specialist evaluation with careful exclusion of alternative diagnoses. Treatment is multimodal including behavioral and educational interventions with the aim to improve cognitive ability, language, and adaptive skills. Medications may be used for adjunct treatment of maladaptive behavior and co-morbid conditions. Prognosis largely depends on degree of intellectual disability, presence of comorbid mental health disorders, and severity of the disease (APA; 2022). Risperidone is an atypical antipsychotic drug. It is useful to target aggressive or self-injurious behaviors, irritability, and outbursts (Luby et.al, 2006). Aripiprazole is of benefit to target symptoms of aggression or self-injurious behaviors, irritability, outbursts, with improvement in speech, hyperactivity, adherence, and stereotypies. Aripiprazole has higher efficacy than other atypical antipsychotics. (Fallah et.al, 2019)

ADHD is common, chronic, pervasive, neurodevelopmental disorder characterized by developmentally inappropriate levels of the core symptoms of hyperactivity, impulsivity, and inattention that adversely affect behavioral, emotional, cognitive, academic, occupational, and social functions (AAP; 2022). Recent guidelines for treatment of ADHD recommend an individualized, multi-modal treatment approach including pharmacological, and non-pharmacological interventions. Available medications are stimulants as methylphenidate, and non-stimulants as atomoxetine. (Mechler et.al, 2022)

Depression and anxiety in childhood can delay normal development by interfering with social, emotional, cognitive, and academic milestones. The number of children and adolescents diagnosed with depression or anxiety has been increasing over time (Bitsko et.al, 2018). About 3% of children have been diagnosed with depression, and prevalence dramatically increases with age (Ghandour et.al, 2019). Psychotherapy recommended as the first-line option for mild to moderate depression that does not include suicidality. Combination psychotherapy and pharmacotherapy is indicated for moderate to severe depression that is resistant to psychotherapy or includes suicidality. (Jackson and Lurie;

2006)

Antipsychotics are thought to inhibit dopamine in the nigrostriatal pathway of the brain, which results in EPS such pseudo parkinsonism, dystonia, and akathisia. Blocking 5-HT<sub>2A</sub> receptors increases the number of dopaminergic neurons in the striatum and reduces the chance of extrapyramidal reactions. Prolactin is released because of dopamine receptor blockage in the tuber-infundibular pathway, with the possibility of hyperprolactinemia (Bostwick et.al, 2009). Risperidone has strong antagonist activity at alpha-1 receptors, which may lead to orthostatic hypotension, as it may cause fainting, syncope, and reflex tachycardia. Risperidone also has a high affinity for H<sub>1</sub> receptors, which could explain the adverse effects like sedation and weight gain. Risperidone has no affinity for cholinergic nor beta-adrenergic receptors. (Sood et.al, 2008)

Side effects are not a side issue. The most important problem of psychopharmacology is non-adherence and one of the most common causes of non-adherence is adverse effects. Adverse effects may exceed the patient suffering from the disease itself. Adverse effects cause suffering and non-adherence that need to be prevented, reduced, and managed. Clinical researchers and funding agencies need to focus substantial research efforts to develop better approaches to assessment, reporting, and management of adverse effects by developing good and effective pharmacovigilance systems (Doghramji and Jangro, 2016). So that, the aim of this study is to describe the side effects of some psychotropic drugs, e.g., risperidone, aripiprazole, atomoxetine, fluoxetine, sertraline, omega-3 and citicoline.

**Methodology:**

The present study is descriptive study, data were collected by asking mothers of CWD about the side effects of psychotropic drugs by using questionnaire modified form the Follow-up sheet of Child and Adolescent Psychiatry Clinic; Center of Care of Children with Special Needs; Faculty of Post-graduate Childhood Studies, Ain-Shams University, Cairo, Egypt. The study included 34 patients who matched with inclusions criteria of being children with special needs, age from 4 to 10 years old, from the period from October 2020 to October 2021; diagnosed by specialists who are psychiatrists and neurologists to whom prescribe psychotropic medications. Ethical approval for the study granted by the Research Ethics Committee, Ain Shams Faculty of Postgraduate Childhood Studies.

**Data Analysis:**

Data analyzed using SPSS version 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). Categorical variables presented as number and percent.

**Results:**

The patients sharing in this study were distributed according to gender; into males (70.6% i.e., 24 out of 34 patients) and females (29.4% i.e., 10 out of 34), as shown in fig. (1).

## Pharmacovigilance of Psychotropic Drugs in Children with Disability

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## Summary

**Introduction:** Pediatrics pharmacovigilance for psychotropic drugs therapy is essential. Treatment with psychotropic drugs in children requires continuous follow up for frequent monitoring of side effects. So that, the aim of this study is to report the side effects of psychotropic drugs. This study is a descriptive study conducted by asking the mothers about side effects of psychotropic drugs using questionnaire modified from the Follow- up sheet of the Child and Adolescent Clinic of Psychiatry; Center of Care of Children with Special Needs, Faculty of Post- graduate Childhood Studies, Ain- Shams University, Cairo, Egypt. The study included 34 patients: with inclusions criteria of being children with special needs, age from 4 to 10 years old. The patients were diagnosed with psychiatric disorders e.g., ASD, ADHD, Depression, OCD.

**Conclusions:** Pharmacovigilance of psychotropic drugs is essential due to their side effects. The most common side effects reported with risperidone are unpalatable, sedation, sleepiness, weight gain, with aripiprazole are anorexia, vomiting, sedation, sleepiness, tremors, fatigue, with atomoxetine are anorexia, nausea, diarrhea, agitation, headache, palpitation, weight loss, with fluoxetine are anorexia, nausea, vomiting, agitation, weight loss, with sertraline are anorexia, nausea, vomiting, insomnia, agitation, headache, and with omega- 3 fatty acids are unpalatable, fishy odor, diarrhea. Minimal GIT upset side effects reported with Citicoline. Pharmacovigilance of psychotropic drugs is a vital process to due to their side effects, so it is important to stabilize the process of pharmacovigilance in integrated management of children with disabilities. Treatment with psychotropic drugs in children and adolescents needs continuous monitoring for adverse drug reactions.

**Abbreviations:** Autism Spectrum Disorder (ASD); Attention- deficit/hyperactivity disorder (ADHD); Children with Disability (CWD); Extrapyramidal symptoms (EPS); Obsessive Compulsive Disorder (OCD); Post- traumatic Stress Disorder (PTSD); selective serotonin reuptake inhibitor (SSRI); Generalized Anxiety Disorder (GAD); Intellectual Disability (ID).

## التيقظ الدوائي للأدوية النفسية عند الأطفال ذوي الاحتياجات الخاصة

**مقدمة:** التيقظ الدوائي في طب الأطفال للعلاج بالعقاقير النفسية أمر ضروري ويتطلب متابعة مستمرة لمراقبة الآثار الجانبية لهذه العقاقير. لذلك، فإن الغرض من هذه الدراسة هو وصف الآثار الجانبية للأدوية النفسية عند الأطفال وخاصة الأطفال ذوي الاحتياجات الخاصة. تم إجراء هذه الدراسة الوصفية؛ باستخدام الاستبيان المعدل على ورقة المتابعة الخاصة بعيادة الطب النفسي للأطفال والمرافقين بمركز رعاية الأطفال ذوي الاحتياجات الخاصة. تم تشخيص المرضى من قبل متخصصين من الأطباء النفسيين وأطباء الأعصاب باضطرابات نفسية مثل طيف التوحد وفرط الحركة وقلة الانتباه والاكتئاب والوسواس القهري. في الدراسة الحالية، تم الإبلاغ عن الآثار الجانبية التالية مع ريسبيريدون؛ مر الطعم، والغثيان والدوخة، والتعاس. واعراض اخرى كالارهاق وزيادة الوزن. وبالنسبة للآثار الجانبية مع أريبيريلازول، فقدان الشهية والغثيان والتعاس والهزات والارتباك والترنح، وأعراض تشبه أعراض الأنفلونزا. ومع أتوموكسينين، فإن الآثار الجانبية على الجهاز الهضمي هي فقدان الشهية والغثيان وآلام البطن والإمساك أو الإسهال. وعلى الجهاز العصبي المركزي: مثل التهيج، والتعب، وغيرها مثل الصداع، وآلام العظام، والخفقان، وفقدان الوزن. ومع فلوكستين فقدان للشهية، وغثيان وقيء والم البطن وتهيج وفقدان الوزن. ومع سيرترالين على الجهاز الهضمي، فقدان الشهية والغثيان الأرق، والإثارة، والعدوانية. واعراض جانبية اخرى مثل؛ شحوب، تعب، أعراض تشبه أعراض الأنفلونزا، صداع. الآثار الجانبية التي تم الإبلاغ عنها مع الأحماض الدهنية أوميغا ٣ مثل طعم ورائحة زيت السمك والإسهال ٥٠%، في حين أن سيتيكولين مستساغ مع الحد الأدنى من الآثار الجانبية. لذا فإن توصيات هذه الدراسة؛ تركز على ضرورة التيقظ الدوائي للأدوية النفسية، وإن الحاجة لإدماج عملية التيقظ الدوائي في الإدارة المتكاملة لعلاج الأطفال ذوي الإعاقة ولتوفير طرق جديدة للإبلاغ عن الآثار الجانبية وكيفية التنبؤ والاكتشاف المبكر وإما لمنع أو علاج هذه الآثار الجانبية.