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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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MITOCHONDRIAL VITIATION CONGRUENTLY APTLY WITH AUTISM SPECTRUM DISORDER

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Abstract.

Background: Mitochondrial dysfunction in autism leads to impair the mitochondria's ability to synthesis adenosine triphosphate (ATP) by impairment citric acid cycle as well as increase anaerobic glycolysis.

Aim: Measuring and evaluating the levels of mitochondrial markers; including glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), malate dehydrogenase, and pyruvate kinase) in the autistic group and knowing the possibility of using these markers to diagnose children with autism spectrum disorder.

Method: A case-control study was done in the Al-Zahraa Teaching Hospital (Kut City, Iraq) on 100 Iraqi children (male and female), between (April 2023 and January 2024). Their ages ranged between 3 and 9 years. Among them were 50 patients enrolled as autistic group and 50 healthy enrolled as control group. Blood samples were collected and bioassays for GOT, GPT, pyruvate kinase, and malate dehydrogenase were measured by ELISA technique.

Results: The autistic group showed that the urine GOT, urine GPT, serum malate, and serum pyruvate levels in the ASD group was significantly higher ($P<0.001$) than the control group. The ROC analysis showed that urine GOT, urine GOT, serum malate and serum pyruvate had an accuracy level of (81%,71%,77%, and 80 %) and the area under the curve (AUC) was > 0.7 (0.8),0.7, 0.7(0.76), and 0.7(0.8) thus urine GOT, urine GPT, serum, malate, and serum pyruvate are a valid diagnostic marker.

Conclusion: There was a significant difference in the mean urine and serum concentrations of mitochondrial markers (GOT, GPT, malate dehydrogenase, and pyruvate kinase) between autistic children and the control group due to mitochondrial dysfunction.

Key words. Autism spectrum disorder, mitochondria, pyruvate, lactate.

Introduction.

One of the most common early child psychiatry and neurology disorders associated with autism spectrum disorder (ASD) are a class of neurodevelopmental disorders defined by qualitative impairments in social functioning and communication, often accompanied by repetitive and stereotyped patterns of behavior and interests [1].

Autism was first described by Kanner in 1943 in a detailed report of 11 children with similar unusual tendencies [2]. The description of the core features of ASD as being social communication deficits and repetitive and unusual sensory–motor behaviours has not changed substantially since its original delineation. However, autism is now seen as a spectrum that can range from very mild to severe [3]. Nevertheless, many (but not all) individuals with ASD require lifelong support of some kind [4].

The prevalence of ASD has dramatically increased in the last decades, reaching estimates of 1 subject in 59 as reported by the Centre for Disease, Control, and Prevention in the US [5]. Every person with an ASD has a unique pattern of behavior, but there are some common signs and symptoms. Communication problems (difficulty using or understanding language) such as delayed speech development and limited vocabulary for their age, repeating a set of words or phrases, focusing attention and conversation on a few topic areas, monotonous and flat speech [6].

Difficulty in social interaction includes having trouble making friends and interacting with people; difficulty understanding facial expressions; difficulty understanding their own and other people's emotions; not making eye contact; not wanting to be cuddled; not answering when called; or refusing to do things when asked [7]. Repetitive behaviors and following strict routines may include repetitive body movement such as hand flapping and repetitive motions with objects like spinning the wheels of a toy car, performing activities that could cause self-harm such as biting or head-banging, sticking to the same routine every day, and having difficulty adjusting to even minor change [8]. Sensory sensitivity Being over- or under sensitive to sounds, lights, touch, tastes, smells, pain, and other stimuli [9].

The ASD has no single known cause [10]. Given the complexity of the disorder and the fact that symptoms and severity vary, there are probably many causes. Mitochondrial dysfunction, genetics, and environment may play a role. Some of the suspected risk factors for autism include genetic mutations, fragile X syndrome, and other genetic disorders; having a sibling with ASD; having older parents; very low birth weight; fetal exposure to the medications valproic acid (Depakene) or thalidomide (Thalomid); exposure to heavy metals and environmental toxins [11,12].

The definition and diagnosis of these disorders has been broadened over the years to include milder forms of autism [13]. The term ASDs are currently used to describe three of the five pervasive developmental disorders listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and the International Classification of Diseases, Tenth Edition (ICD-10): autistic disorder, Asperger disorder and pervasive developmental disorder-not otherwise specified (PDD-NOS) [14].

Mitochondrial dysfunction in autism leads to impair the mitochondria's ability to synthesis ATP by impairment citric acid cycle as well as increase anaerobic glycolysis [15]. Thus, affect level of biochemical markers of mitochondrial dysfunction and

include glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), lactate, pyruvate, lactate-to-pyruvate ratio, malate, ubiquinone, alanine, alanine-to-lysine ratio, and acyl-carnitine [16]. The present study aimed for measuring and evaluating the levels of mitochondrial markers (GOT, GPT, malate dehydrogenase, and pyruvate kinase) in autistic group.

Materials and Methods.

Study design: A case-control study was done in the Al-Zahraa Teaching Hospital (Kut City, Iraq) on 100 Iraqi children (male and female), between (April 2023 and January 2024). Their ages ranged between 3 and 9 years. Among them were 50 patients enrolled as autistic group and 50 healthy enrolled as control group. Children are diagnosed by physicians who are specialized in this field and written informed consent was obtained from all family patients for participation in the study. Blood samples were collected and bioassays for GOT, GPT, pyruvate kinase, and malate dehydrogenase were measured by ELISA technique [17,18].

Blood sample collection: Five milliliters of blood for each participant were collected from vein puncture in sterile gel tubes and allowed to clot for a few minutes at room temperature, followed by separation of the serum from the clot by centrifugation for 10 minutes at a 2012 x g. Then they were divided into several Eppendorf tubes and immediately frozen at -80°C until used in the bioassays.

Urine sample collection: Ten milliliters of urine (medium stream urine) were collected in a plastic collection vessel. Then, the samples were temporarily kept in an ice box and transported to the laboratory. Urine samples were quickly sent to the laboratory for the purpose of study and laboratory examinations.

Inclusion Criteria: Children had ASD.

Exclusion Criteria: Children were not included if they had ASD with a neurological disease such as Alzheimer's disease, epilepsy, schizophrenia, or any other illness that may defect in the nervous system.

Biochemical analysis: The reagents preparation and assay procedure were carried out according to manufacturer description using ELISA kit supplied by BT LAB (China).

Statistical analysis: The results were conducted according to GraphPad prism 9.2.1 used to gather, summarize, analyze, and present data. ANOVA was used to assess the significance of differences between groups and within times. The data were expressed as mean ± standard deviation (SD) and P value<0.05 was considered statistically significant, while P-values equal to or less than 0.01 were considered high significance using T-test and Tukey multiple comparisons. Pearson correlation coefficient was used to estimate the correlation and Receiver operating characteristic (ROC) test were used to quantify the degree of significance, which is displayed through the estimation plot.

Results.

Demographic characteristics: There was no significant variation in the proportion of males and females between the control group and the ASD group (p = 0.98). However, the proportion of males in the ASD group was higher than the proportion of females: 41 (82 %) males versus 9 (18 %) females, indicating that males are more likely to be affected than females (Table 1). There was no significant difference in mean age between the control group and ASD group (p = 0.73), while there was a significant variation in the age proportion between control group and ASD group (p<0.01), respectively (Table 1).

Table 1. *Comparison of demographic characteristics between control group and ASD group.*

Characteristic	**Control**		**ASD**		***P***
Gender	**Male**	**Female**	**Male**	**Female**	
	N (38)	**N (12)**	**N (41)**	**N (9)**	**0.98**
	76%	**24%**	**82%**	**18%**	**NS**
Age (years)					
Mean ±SD	6.40±1.67		6.52±1.83		0.73
Range	3-9		3-9		NS
3-5 years	N (12) 24%	N (3) 6%	N (11) 22%	N (6) 12%	p < 0.01
6-7 years	N (10) 20%	N (7) 4%	N (18) 36%	N (0) 0%	
8-9 years	N (16) 32%	N (2) 14%	N (12) 24%	N (3) 6%	

N: number of cases; P: probability value; NS: not significant; ASD: autism spectrum disorder; SD: standard deviation

Mitochondrial parameters: The results of measuring urine GOT levels (ng/ml) in the autistic group showed that the urine GOT level in the ASD group was significantly higher (P<0.001) than the control group. The results of measuring urine GPT levels (ng/ml) in the autistic group showed that the urine GPT level in the ASD group was significantly higher (P<0.001) than the control group. The results of measuring serum malate levels (ng/ml) in the autistic group showed that the serum malate level in the ASD group was significantly higher (P<0.001) than the control group. The results of measuring serum pyruvate levels (ng/ml) in the autistic group showed that the serum pyruvate level in the ASD group was significantly higher (P<0.001) than the control group (Figure 1).

Correlation study: The GOT, GPT, and malate showed no significant correlation to age (p > 0.05), while pyruvate showed a significant positive correlation to age (R = 0.279, P = 0.049) (Figure 2).

There was a significant positive correlation between GOT and GPT (R = 0.332, P = 0.019), while malate showed no significant correlation to GOT (p > 0.05). In addition, there was a significant negative correlation between GOT and pyruvate (R = -0.307, P = 0.030). Malate, and pyruvate showed no significant correlation to GPT (p > 0.05). Pyruvate showed no significant correlation to malate (p > 0.05) (Figure 3).

Receiver operating characteristic (ROC) curve: The existence of a significant difference in mean urine GOT, urine GPT, serum malate, and serum pyruvate between the ASD and healthy (control) groups suggests a possible predictive role for these markers in the early diagnosis of ASD; therefore, receiver operator characteristic (ROC) curve analysis was performed. The ROC analysis showed that urine GOT had an accuracy level of 81%, and the area under the curve (AUC) was > 0.7 (0.8), thus urine GOT is a valid diagnostic marker. Also, ROC analysis showed that urine GPT had an accuracy level of 71% and the area under the curve (AUC) was 0.7, thus urine GPT is a valid diagnostic marker. On other hand, ROC analysis showed

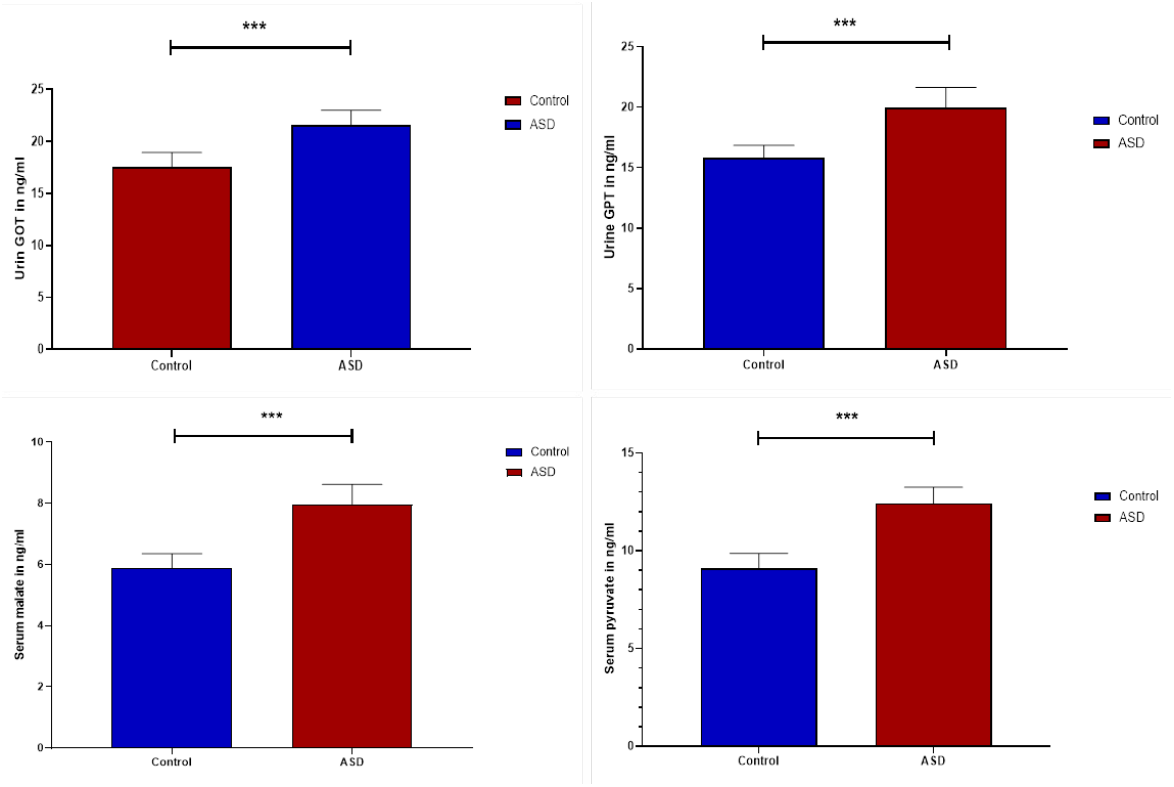

Figure 1. *Comparison of mean serum pyruvate between control group and ASD group shows significant difference.*

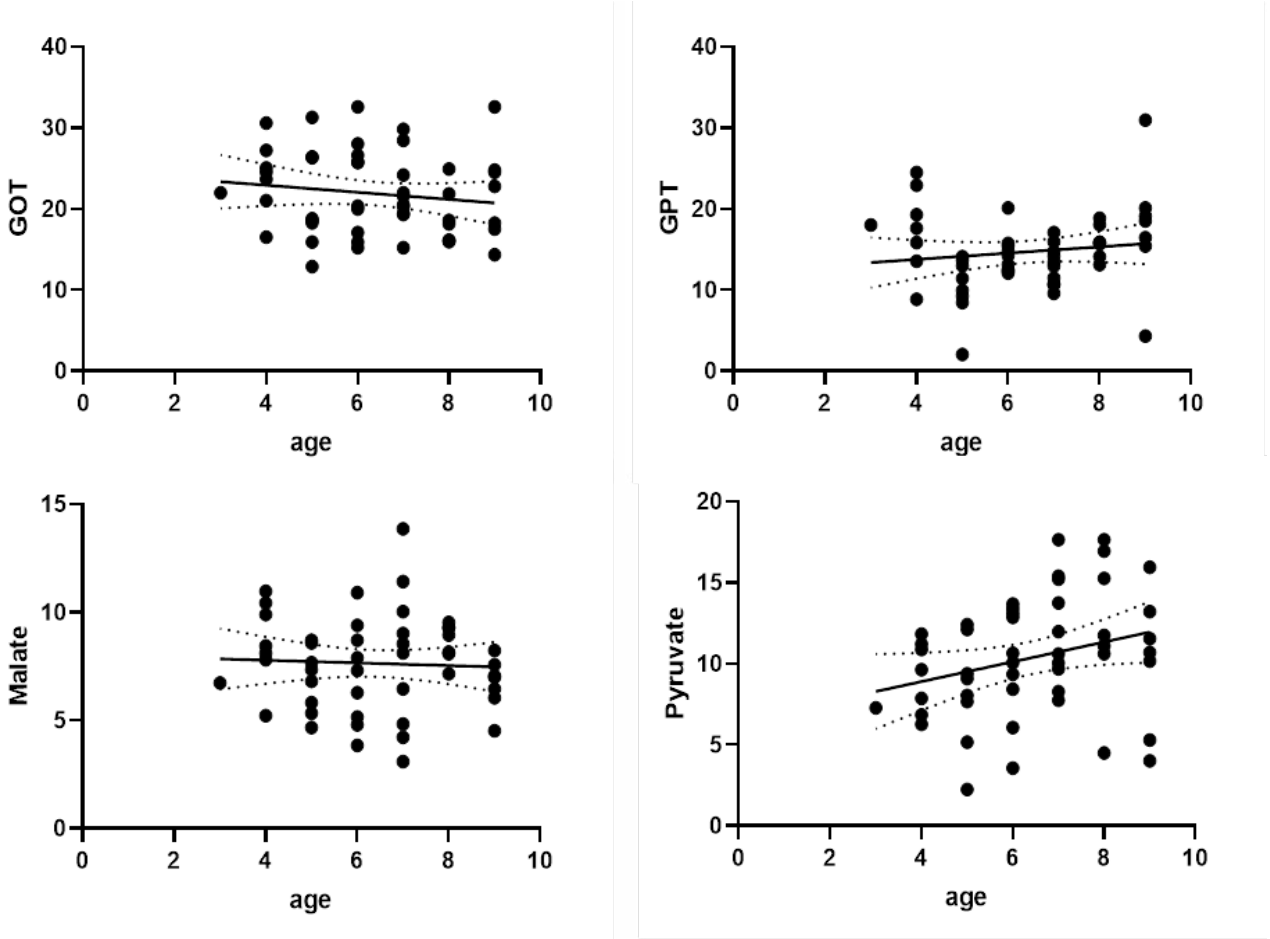

Figure 2. *The correlation between age with GOT, GPT, malate, and pyruvate.*

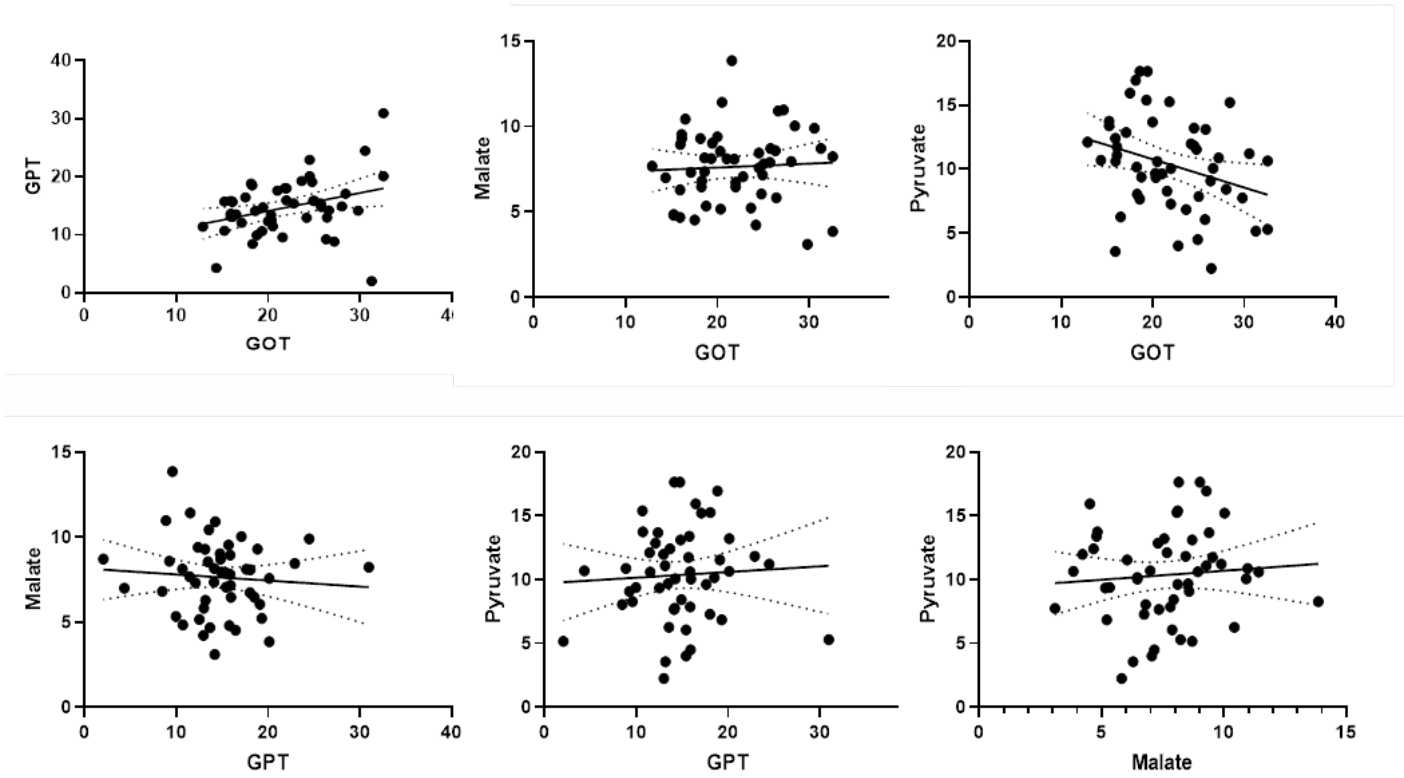

Figure 3. *The correlation between the measured biochemical parameters.*

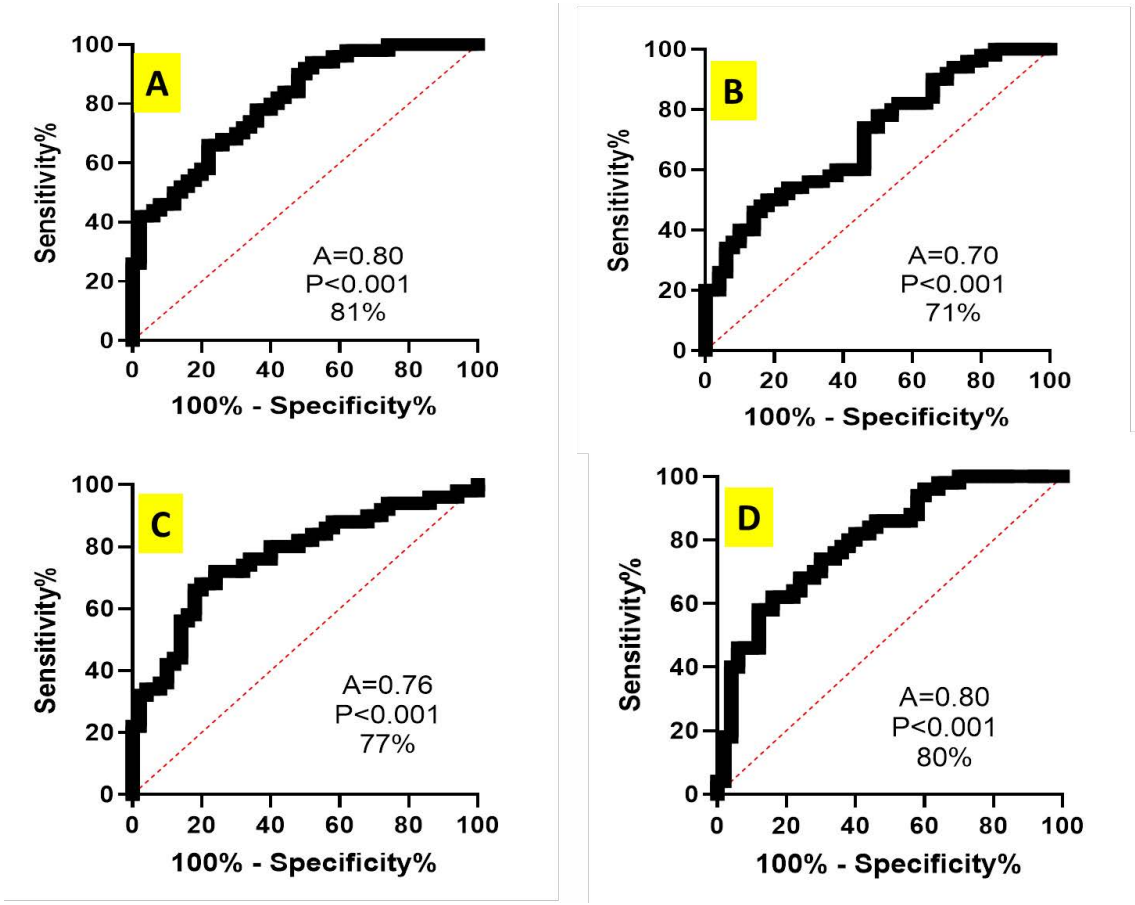

Figure 4. *Receiver operating characteristic (ROC) curve for the results of (A) urine GOT, (B) urine GPT, (C) serum malate, and (D) serum pyruvate levels, plotting the sensitivity and specificity of each biochemical marker.*

that serum malate had an accuracy level of 77%, and the area under the curve (AUC) was > 0.7 (0.76), thus serum malate is a valid diagnostic marker. Also, ROC analysis showed that serum pyruvate had an accuracy level of 80 %, and the area under the curve (AUC) was > 0.7 (0.8), thus serum pyruvate is a valid diagnostic marker (Figure 4).

Discussion.

ASD is a neurodevelopmental disorder characterized by deficits in social communication and the presence of restricted interests and repetitive behaviors. Recent changes to the diagnostic criteria occurred with the transition to the new diagnostic manual (DSM-5) and will likely impact prevalence, which currently stands at 1 in 59 children in the US [10]. ASD is a neurobiological disorder influenced by both genetic and environmental factors affecting the developing brain. Research continues to reveal factors that correlate with ASD risk and these findings may guide further etiologic investigation, but no final causal pathway has been elucidated [19]. Clinical evaluation begins with developmental screening of the general pediatric population to identify at-risk children, followed by referral to a specialist for a definitive diagnosis and comprehensive neuropsychological assessment [20]. Children with ASD should also be screened for common co-morbid diagnoses [21]. Mitochondrial dysfunction has been implicated in several psychiatric and neurological disorders. Over 20 years ago, Coleman and Blass hypothesized that individuals with ASD may have an abnormality in carbohydrate metabolism, and in 1998 Lombard proposed that ASD may be a disorder of impaired mitochondrial function [22,23]. Over the past decade, evidence has accumulated that some individuals with ASD have concomitant mitochondrial dysfunction, and some have proposed a 'mitochondrial autism' subgroup. Several review articles have been recently published concerning mitochondrial dysfunction in ASD [24]. The mitochondrial disorders are characterized by various clinical, biochemical, molecular, and histological features. Biochemical parameters for mitochondrial dysfunction include increased aspartate GOT and GPT [25].

The high level of GOT and GPT according to the data presented in this study is compatible with several studies that found a significant increase in the levels of GOT and GPT [26,27]. Mitochondrial dysfunction raises levels of aspartate aminotransferase and alanine aminotransferase [28]. Mitochondrial dysfunction causes disturbance of the TCA cycle, which reduces the aerobic respiration rate, and this phenomenon generally results in elevated levels of pyruvate as well as its derivatives, lactate, and alanine. Pyruvate is converted to alanine by GPT, whereas the pyruvate-derivative oxaloacetate is converted to aspartate by the GOT enzyme [29]. A study at 2022 was done on 200 children aged 7 to 9 years showed that GOT and GPT values were highly significant in the ASD children group as compared with the healthy group [30]. Also, a study was carried out on 146 Egyptian found markers of mitochondrial dysfunction GOT and GPT were elevated in autistic children group [31]. The data of previous study is consistent with the data present in this study were GOT and GPT level are significantly high in autistic children.

The present study showed that the serum malate dehydrogenase level is significantly higher in autistic patients, which may be due to mitochondrial dysfunction. As the energy factories of cells, mitochondria are the main sites for the generation of ROS, in which the electron transport chain (ETC) is a prime source for ROS. Both endogenous and exogenous oxidative stress can cause a deficit in mitochondrial ETC complexes, resulting in mitochondrial dysfunction [32,33]. ROS production by mitochondria can lead to oxidative damage to mitochondrial proteins, membranes and DNA, impairing the ability of mitochondria to synthesize ATP and carry out their wide range of metabolic functions, including the tricarboxylic acid cycle, fatty acid oxidation, the urea cycle and amino acid metabolism. Inhibition of the TCA cycle may result in an elevation of TCA cycle intermediates [34], which may disturb the level of mitochondrial malate in neurological disorder [35].

Mitochondrial dysfunction impairs aerobic respiration, leading to a reduction in TCA cycle function resulting in an elevation in pyruvate [36]. A recent study has observed a significant increase in LDH-A expression and pyruvate levels in ASD [37]. Up to now, few studies have described the expression of the different glycolytic enzymes in ASD [38-40]. However, several studies have shown elevated lactate levels in ASD patients. In the same way, production of pyruvate is stimulated [41,42]. These findings may suggest an elevation of glycolysis through the phenomenon of anaerobic glycolysis in ASD since the dysregulation of this balance has been proposed as a candidate cause of ASD [37]. All previous studies were consistent with the data of the present study, which showed the serum pyruvate kinase level was significantly higher in the autistic group.

In this study, it was found that the proportion of male with ASD is, higher (82%) compared to females (18%), indicating that males are more likely to be affected than females. Since autism is a largely genetic and hereditary condition, genetic factors that lead to differences depending on sex come into play, such as the role of androgen signalling in male development or X-linked mutations, whose associated genetic conditions are typically more common and severe in males [43]. Findings of present study was supported by several studies [44,45].

Conclusion.

A striking contrast emerged in the average levels of mitochondrial markers (GOT, GPT, malate dehydrogenase, and pyruvate kinase) found in the urine and serum of autistic children compared to the control group, pointing towards the presence of mitochondrial dysfunction.

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