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Comparing Blood glucose changes in PICU patients with and without COVID-19

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Abstract

Background: Since the COVID-19 pandemic began around the world, many studies have been conducted on various aspects of the disease in adults and children, but limited research has been done on blood glucose changes caused by COVID-19. So, this study was conducted to investigate blood glucose changes in children with COVID-19 hospitalized in the pediatric intensive care unit (PICU), comparing it with children hospitalized for other reasons.

Methods: This case-control study was performed on 30 COVID-19 children (group 1) during the pandemic and 29 children (group 2) who were admitted to PICU, before the prevalence of COVID-19. The control group was the same as the case group regarding age, sex, length of hospitalization, and treatment measures. Children with metabolic diseases and malignancy were excluded from the study. The data were analyzed by SPSS version 26 using chi-square and independent t-tests.

Results: Out of 59 participants, two patients had low blood sugar (BS), and one had high BS; notably, all three were in group 1. This difference was not statistically significant. Furthermore, 76.7% of children with COVID-19 and 86.2% of the other group had normal BS. The frequency distribution of BS levels in the two groups was not related to the age, gender, and hospitalization period of children.

Conclusion: This study revealed that children with COVID-19 hospitalized in PICU did not have significant BS changes compared to those hospitalized before the pandemic. In addition, gender, duration of hospitalization, and COVID-19 medication did not significantly affect blood sugar changes.

Key Words: Blood Glucose, Children, COVID -19, Pandemic, Pediatrics, PICU.

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1- INTRODUCTION

Since December 2019, the rapid spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from China has caused a novel pneumonia called COVID-19 (1, 2). The World Health Organization (WHO) declared it as a public health emergency of international concern (3). Some studies have shown that this disease appears mostly asymptomatic or mild in affected children (4).

According to the studies conducted in China, 86.6% of COVID-19 cases were over 30 years old, and 2.1% were under 20. (5) Children under five years of age are more likely to be infected with a severe form of COVID-19 (3-6).

COVID-19 has uncertain effects on multiple organs. Also, the impact of this disease on endocrine systems has not been studied, and its specific metabolic side effects have yet to be entirely determined. (7)

Diabetes can affect the immune response to pathogens and thus make patients more vulnerable to infections. Diabetic patients are at higher risk of infection than healthy controls; and this is even higher in Type 1 diabetes mellitus (T1D) children than in those with Type 2. (8)

BS control is crucial in patients with COVID-19 and those without it (9). The relationship between diabetes mellitus and its harmful outcomes in viral infections is not unexpected because the increase in BS is decisive in controlling viremia, inflammation, and the mortality of patients (10).

Appropriate control of BS is closely related to improving clinical outcomes in patients with COVID-19 (11, 12). However, the extent of the impact of the severity of COVID-19 on the effective parameters of BS and HBA1C is unknown (13). One study demonstrated that COVID-19 leads to increased BS in patients with no history of diabetes and use of glucocorticoids (14). There is an unknown relationship between the severity of COVID-19 and increased BS, especially in children, so the infection of COVID-19 may lead to insulin resistance by creating stress and increasing pro-inflammatory cytokines (11). In one study, acute hyperglycemia in the intensive care unit was reported to be more dangerous for people without diabetes than with it (12). Some studies have suggested that the pancreas may be the target of the SARS-CoV-2 virus, so this virus damages the endocrine glands of the pancreas. And it can lead to acute insulin-dependent diabetes (13, 14). This issue is probably one reason for BS increase in patients with COVID-19 without a previous history of diabetes (11). Insulin resistance may also be another reason for increased BS in patients with COVID-19 (12). A study in China indicated a strong relationship between the severity of COVID-19 and BS (11). However, in some other studies, the increase in BS was reported independent of the history of diabetes (15, 16).

Although several studies have been conducted on BS changes in adults with COVID-19 since the pandemic's beginning, children have received less attention in this field. There is very little data on BS changes in children under 18 years of age during the pandemic. We conducted the present study to compare the average BS and its changes in children under 18 years of age with COVID-19 hospitalized in the PICU.

2- MATERIALS AND METHODS

In this case-control study, the information related to children hospitalized in the PICU department was extracted from the children's research database of Shahid Sadoughi Hospital in Yazd. The data included age, gender, medication, clinical symptoms, duration of hospitalization, invasive procedures, and COVID-19 status for the case group

(suspected, definite, probable). The case group of this study included The PICU patients with COVID-19 and the control group composed of all children under 18 years of age with negative COVID-19 hospitalized in PICU from January 2019 to March 2021.

The target population included 59 children hospitalized in PICU, of which the census selected 30 children with COVID-19 from February 2020 to July 2021(group 1), and the rest were hospitalized with negative COVID-19 (group 2). The control group was matched with the case group regarding age, gender, length of hospitalization, and treatment. Patients with metabolic diseases or malignancy were excluded from the study. The mean BS level of 100-140 mg/dl was considered normal, 140-200 mg/dl suspicious, above 200 mg/dl hyperglycemia, and below 50 mg/dL hypoglycemia. The drugs used in patients with COVID-19 (group 1) included corticosteroids and remdesivir. The information was coded and analyzed by SPSS version 26, using mean and standard deviation, chi-square, and independent t-test, at a significance level of P value <0.05.

3- RESULT

Out of 59 studied children, 30 were in group 1, and 29 were in group 2. The results of the present study showed that the classification of BS does not differ between the two groups of PICU children. The present study's findings showed that in children hospitalized during the COVID-19 pandemic, BS was normal in 76.7% of cases. In contrast, in the control group, 86.2% of children had normal BS before the pandemic (P-value = 0.381). Although height and low BS level were observed only in group 1, this difference was not statistically significant (**Table 1**).

Table-1: Comparing frequencies of BS changes in two groups

Time	Low	Normal	Suspicious	High	Total
Group 1	2 (6.7%)	23 (76.7%)	4 (13.3%)	1 (3.3%)	30 (100%)
Group 2	0 (0%)	25 (86.2%)	4 (13.8%)	0 (0%)	29 (100%)

The frequency distribution of BS levels in both groups was not related to the age, gender, and hospitalization period of children (**Table 2**).

We observed hypoglycemia only in group 1 in both genders, and the chi-square test did not show a significant difference (P-value>0.05). In addition, hyperglycemia was reported only in one patient in group one, which did not lead to a significant difference between the groups (**Table 2**).

4- DISCUSSION

To our knowledge, this is the first study that compares mean blood sugar and its changes in PICU children during infection by COVID-19 with the non-infected ones, before the pandemic. We did not find a remarkable change in the mean BS levels of the case and control groups of children. The mean BS levels in both groups were approximately the same. A Chinese study conducted on 221 adults with COVID-19 declared that severe COVID-19 infection was extraordinarily associated with increasing BS. They reported that BS was remarkably higher in patients with severe COVID-19 than in those with mild COVID-19 (10). In addition, Zhang et al. indicated that those not diagnosed with diabetes experienced an increase in BS after exposure to COVID-19 (12). Furthermore, they reported that 18 out of 21 severe COVID-19 infected cases without diabetes had very high BS rates (13).

Table-2: Frequencies of BS changes in two groups based on demographic information, length of hospitalization, and drug use

Variable		Time	Blood Sugar					P-value*
			Low	Normal	Suspicious	High	Total	
Gender	Boy	Group1	1 (5.3%)	14 (73.7%)	3 (15.8%)	1 (5.3%)	19 (100%)	0.54
		Group 2	0 (0%)	16 (84.2%)	3 (15.8%)	0 (0%)	19 (100%)	
	Girl	Group 1	1 (9.1%)	9 (81.8%)	1 (9.1%)	0 (0%)	11 (100%)	0.62
		Group 2	0 (0%)	9 (90%)	1 (10%)	0 (0%)	10 (100%)	
Duration of hospitalization	<7 day	Group 1	2 (13.3%)	10 (66.7%)	2 (13.3%)	1 (6.7%)	15 (100%)	0.26
		Group 2	0 (0%)	15 (83.3%)	3 (16.7%)	0 (0%)	18 (100%)	
	7-14 day	Group 1	0 (0%)	7 (77.8%)	2 (22.2%)	0 (0%)	9 (100%)	0.15
		Group 2	0 (0%)	8 (100%)	0 (0%)	0 (0%)	8 (100%)	
	>14 day	Group 1	0 (0%)	6 (100%)	0 (0%)	0 (0%)	6 (100%)	0.13
		Group 2	0 (0%)	2 (66.7%)	1 (33.3%)	0 (0%)	3 (100%)	
Age	<1 year	Group 1	2 (25%)	5 (62.5%)	1 (12.5%)	0 (0%)	8 (100%)	0.32
		Group 2	0 (0%)	5 (71.4%)	2 (28.6%)	0 (0%)	7 (100%)	
	1-3 year	Group 1	0 (0%)	8 (100%)	0 (0%)	0 (0%)	8 (100%)	0.15
		Group 2	0 (0%)	7 (77.8%)	2 (22.2%)	0 (0%)	9 (100%)	
	3-5 year	Group 1	0 (0%)	3 (75%)	1 (25%)	0 (0%)	4 (100%)	0.23
		Group 2	0 (0%)	5 (100%)	0 (0%)	0 (0%)	5 (100%)	
	5 -13 year	Group 1	0 (0%)	6 (66.7%)	2 (22.2%)	1 (11.1%)	9 (100%)	0.23
		Group 2	0 (0%)	7 (100%)	0 (0%)	0 (0%)	7 (100%)	
	13-18	Group 1	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	NA
		Group 2	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	
Drug usage	With drug	Group 1	0(0%)	7(30.4%)	1(25%)	0(0%)	8(26.7%)	0.73
	Without drug	Group 1	2(100%)	16(69.6%)	3(75%)	1(100%)	22(73.3%)	

Another study found that patients with new-onset hyperglycemia caused by stress or COVID-19 infection had poorer outcomes than those with normoglycemia or pre-existing diabetes (14).

Several studies have reported changes in BS, especially hyperglycemia, proposing several mechanisms in adults. It is explained that the SARS-CoV and SARS-CoV-2 attach themselves to the host cell's angiotensin-converting enzyme 2 (ACE2) receptors and invade the cells (15). Many human organs, including the respiratory tract and the heart, show the ACE2 protein (16). A study proposed that immunostaining in islets is stronger than in exocrine tissues, suggesting that ACE2 protein may be present in islet B cells, causing hyperglycemia through the destruction of these cells (17).

Notably, there was a worse outcome for COVID-19 patients with hyperglycemic disorders. A recent study reported that most cases of hyperglycemia were men. ACE2 protein expression was almost three times higher in men than in women. (18)

But in children, consistent with our results, less hyperglycemia has been reported in patients with COVID-19; maybe the mechanisms proposed in adults are not activated in children.

4-1. Limitations of the study

The present study had several limitations:

a) It was conducted in a single center and used a retrospective design.

b) The sample size was relatively small. Further research with a large sample size is, thus, necessary to confirm our results.

c) Studies with detailed glycemic parameters to determine the severity of COVID-19 were limited, and we could compare our findings with those of other studies.

d) Treatments and medications used during infection by COVID-19 are not obvious.

Probably, it may impact the finding of studies.

5- CONCLUSION

This study demonstrated that children with COVID-19 hospitalized in PICU did not have significant BS changes compared to those hospitalized before the pandemic. In addition, gender, duration of hospitalization, and COVID-19 medication did not significantly affect blood sugar changes.

6- FUNDING

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8- CONFLICT OF INTEREST:

None.

9- REFERENCES

1. Liu X, Na R, Bi Z. Challenges to prevent and control the outbreak of Novel Coronavirus Pneumonia (COVID-19). Zhonghua liu xing bing xue za zhi= Zhonghua liuxingbingxue zazhi. 2020; 41:E029-E.

2. Team E. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. China CDC weekly. 2020; 2(8):113.

3. Zheng F, Liao C, Fan Q-h, Chen H-b, Zhao X-g, Xie Z-g, Li XL, Chen CX, Lu XX, Liu ZS, Lu W, Chen CB, Jiao R, Zhang AM, Wang JT, DingXW, Zeng YG, Cheng LP, Huang QF, Wu J, Luo XC, Wang ZJ, Zhong YY, Bai Y, Wu XY, Jin RM. Clinical characteristics of children

with coronavirus disease 2019 in Hubei, China. Current medical science. 2020; 40(2):275-80.

4. Nikolopoulou GB, Maltezou HC. COVID-19 in children: where do we stand? Arch Med Res. 2022; 53(1):1-8. doi: 10.1016/j.arcmed.2021.07.002.

5. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. The Lancet infectious diseases. 2020; 20(6):689-96.

6. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, Liu X, Wei L, Truelove SA, Zhang T, Gao W, Cheng C, Tang X, Wu X, Wu Y, Sun B, Huang S, Sun Y, Zhang J, Ma T, Lessler J, Feng T. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. The Lancet infectious diseases. 2020; 20(8):911-9.

7.Chekhlabi N, Haoudar A, Echcharii N, Ettair S, Dini N , New-Onset Diabetes with Ketoacidosis Precipitated by COVID-19 in Children: A Report of Two Cases , Case Rep Pediatr. 2021 Jul 16; 2021:5545258. doi: 10.1155/2021/5545258. E Collection 2021.

8. Shi Y, Wu LQ, Wei P, Liao ZH. Children with type 1 diabetes in COVID-19 pandemic: Difficulties and solutions. World Journal of Clinical Pediatrics, 2022, 11.5: 408.

9. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020; 14(4):303-10.

10. Forbes A, Murrells T, Mulnier H, Sinclair AJ. Mean HbA1c, HbA1c variability, and mortality in people with diabetes aged 70 years and older: a retrospective cohort study. The lancet Diabetes & endocrinology. 2018; 6(6):476-86.

11. Chen J, Wu C, Wang X, Yu J, Sun Z. The Impact of COVID-19 on Blood Glucose: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2020; 11:574541.

12. Zhang Y, Li H, Zhang J, Cao Y, Zhao X, Yu N, Gao Y, Ma J, Zhang H, Zhang J, Guo X, Liu X. The clinical characteristics and outcomes of patients with diabetes and secondary hyperglycaemia with coronavirus disease 2019: A single-center, retrospective, observational study in Wuhan. Diabetes Obes Metab. 2020; 22(8):1443-54.

13. He B, Wang J, Wang Y, Zhao J, Huang J, Tian Y, Yang C, Zhang H, Zhang M, Gu L, Zhou X, Zhou J. The Metabolic Changes and Immune Profiles in Patients with COVID-19. Front Immunol. 2020; 11:2075.

14. Singh AK, Singh R. Hyperglycemia without diabetes and new-onset diabetes are both associated with poorer outcomes in COVID-19. Diabetes Res Clin Pract. 2020; 167:108382.

15. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J Virol. 2020; 94(7).

16. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, Zhu H, Zhao W, Han Y, Qin C. From SARS to MERS, Thrusting Coronaviruses into the Spotlight. Viruses. 2019; 11(1).

17. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol. 2010; 47(3):193-9.

18. Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, Yu X, Dong K. Clinical characteristics and outcomes of patients with severe COVID-19 with diabetes. BMJ Open Diabetes Res Care. 2020; 8(1).