Cardiology in the Young

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Preoperative monocytosis is predictable at diagnosis for RT-PCR negative COVİD-19 paediatric cardiac surgery patients

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Abstract

Other markers investigated in this population have gained importance in the diagnosis of the disease since the course of COVID-19 disease is atypical in the paediatric population and PCR may be misleading. The leukocyte profile is one of these biochemical tests. Children did not have lymphopenia in hemogram count, whereas relatively neutropenia and monocytosis were detected, unlike the adult population. The reason why children do not have lymphopenia is thought to be due to the fact that the thymus is more active in the first years of life.

Two-hundred and four patients operated in our paediatric cardiac surgery clinic from 11March, 2020 to 1 April, 2021 were retrospectively examined and 11 patients with preoperative asymptomatic and PCR (−), but with PCR (+) in the post-operative period (patients with incubation period or false PCR negativity) were included in our study. Patients requiring emergency operation and operated from PCR (+) patients in the preoperative period were excluded from the study.

The neutrophil ratio in the lymphocytic series of 7 patients out of 11 patients was slightly below the normal range in the preoperative period, the lymphocyte ratio of 3 patients was slightly above the normal range, and the relative monocyte ratio of 10 patients was slightly above the normal range.

We think that evaluating the leukocyte profile combined with RT-PCR will give more accurate results in the diagnosis of incubation period and false RT-PCR negative patients. In addition, we believe that the algorithms for non-complex paediatric cardiac surgery procedures and timing in the paediatric population with a better course of COVID-19 disease with a positive post-operative course.

It is known that children are as likely to be infected as adults in the future even though cases are rare in children and newborns in the initial stages of the COVID-19 pandemic. However, the disease is less symptomatic and severe in the paediatric population.[1–3]

A number of mandatory changes have been made in the timing, planning, and technical stages in order to protect the patient and the health system for the operations of patients with CHD who need paediatric heart surgery.[4]

What needs to be done to prevent COVID-19 transmission is identifying infected people by carrying out as many tests as possible and ensuring the isolation of these patients, besides paying attention to personal protective equipment and social distancing. The performance of SARS-CoV-2 diagnostic tests and clinical interpretation of the results are of great importance at this point.[5]

Leukocyte profile, which is a marker investigated in this population, has gained importance since the course of COVID-19 disease is atypical in the paediatric population. Children did not have lymphopenia, whereas relatively neutropenia and monocytosis were detected, unlike the adult population. The reason why children do not have lymphopenia is thought to be due to the fact that the thymus is more active in the first years of life.[6]

PCR test was performed in the preoperative period for all patients and their companions after the onset of the pandemic. Eleven patients with normal asymptomatic and acute phase reactants and negative PCR were positive for COVID-19 PCR in the early post-operative period as a result of these tests. We will share our experience, prognosis, and opinions with you in this patient group.

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Figure 1. Pulmonary images of the patient operated due to Fontan and ECMO inserted after post-operative COVID-19 positivity.

Figure 2. Pulmonary images of the patient operated due to arch hypoplasia and in need of post-operative prolonged mechanical ventilation.

Materials and methods

Our study is a retrospective, observational, single-centre case series study. Two-hundred and four patients operated in our paediatric cardiac surgery clinic from 11 March, 2020 to 1 April, 2021 were retrospectively examined and 11 patients with preoperative asymptomatic and PCR (−), but with PCR (+) in the post-operative period were included in the study. Patients requiring emergency operation and operated from PCR (+) patients in the preoperative period were excluded from the study. Age, gender, weight, diagnosis, previous operations, procedure performed, biochemistry results, and PCR results of the patients were recorded.

All patients underwent PCR and PAAG for a maximum of the last 48 hours before admission to the hospital. The PAAG was interpreted by a radiologist. Blood tests and complete urinalysis were performed. Infection results were evaluated by a paediatrician by questioning the contact history. Patients who were not considered for infection and had no contact in the first place were hospitalised. Those who were hospitalised too urgently to wait for the test results were considered positive and isolated until the test results. All patients were followed up in single rooms. PCR test was repeated in all patients with symptoms of infection such as high fever, intense secretion, and cough in the post-operative period. Patients who were positive as a result of the COVID-19 PCR test were isolated.

The use of Personal Protective Equipment was ensured and the entrances and exits to the operating room were reduced as much as possible after the patient transfer in the operating room. FFP2/FFP3 mask, face protection, liquid-proof apron were used during intubation. FFP2/3, face shields/safety goggles were used as PPE in each operation considering possible false negativities during the pandemic period. Surgeons completed the operations wearing protective gloves. The intubations were performed by the most experienced person in the team with the help of video-supported laryngoscopes and intubation cabinets. Aspiration was performed with closed aspiration systems. A virus filter was inserted into the intubation tubes of the patients in intubated patient transport.

A total of 20 mg/kg vitamin C and vitamin D were added to the post-operative treatments of all patients in addition to surgical antibiotic prophylaxis.

Number Cruncher Statistical System 2007 software (Kaysville, Utah, United States of America) was used for statistical analysis. Descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, Maximum) were used to evaluate the study data. Retrospectively, ethical rules were followed according to the Declaration of Helsinki.

Results

Two-hundred and four patients were operated in our clinic from 11 March, 2020 to1 April, 2021. COVID-19 PCR (+) was detected in the PCR test taken after 11 patients with preoperative asymptomatic and PCR (−) had signs of infection in the post-operative period (5.39%).

Seven of the patients were female and 4 patients were male. The ages of the 11 patients included ranged from 4 to 187 months with a mean of 62.45 ± 64.38. Patients' weight ranged from 3.5 to 42 kg with a mean of 18.22 ± 13.43. Cardiopulmonary bypass was used in all but 1 patient (n:10).

Cardiopulmonary bypass time of the patients ranged from 0 to 155 minutes with a mean of 87.72 ± 41.01. The duration of the cross-clamp is 0–138 minutes. The mean was 65.71 ± 44.15 minutes. One patient needed ECMO (9.09%). It was observed that our mortality rate was 9.09% (n:1). The length of stay in the ICU ranged from 2 to 51 days with a mean of 10.18 ± 15.54. Ventilator time was 1–41 days. The mean ventilator time was 7.45 ± 13.69 days. The ward follow-up period was between 0 and 20 days. 9 ± 5.25 (Figs. 1 and 2).

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Table 1. The table containing the operations and post-operative information of the patients.

Patient No.	Age (months)	Gender	Diagnosis	Operation	CPB (minutes)	CC (minutes)	ICU time (days)	Ventilator time (days)	Ward time (days)	ECMO	Death
1	15	M	AORTIC COARCTATION	END-TO-END ANOSTOMOSIS	0	0	2	1	7	NO	NO
2	49	M	VSD	VSD CLOSURE	108	83	2	1	9	NO	NO
3	5	M	ASD–VSD	ASD–VSD CLOSURE	105	74	3	1	6	NO	NO
4	6	F	VSD–ARCH HYPOPLASIA	ARCH RECONSTRUCTION–VSD CLOSURE	155	141	51	41	20	NO	NO
5	74	F	VSD	VSD CLOSURE	90	72	2	1	7	NO	NO
6	187	F	EBSTEIN'S ANOMALY	CONE REPAIR	124	108	8	2	15	NO	NO
7	146	F	ASD–VSD	ASD CLOSURE	55	24	2	1	7	NO	NO
8	51	F	SINGLE-VENTRICLE PATOLOGY	FONTAN NORWOOD STAGE 3	62	0	28	28	0	YES	YES
9	20	F	TETRALOGY OF FALLOT	TOTAL CORRECTION	111	98	8	3	11	NO	NO
10	130	M	AORTIC RIDGE	RIDGE RESECTION	84	71	3	2	6	NO	NO
11	4	F	VSD–PDA	VSD–PDA CLOSURE	71	52	3	1	11	NO	NO

ASD = atrial septal defect; CC = cross-clamp; CPB = Cardiopulmonary bypass; ECMO = Extracorporeal membrane oxygenation; ICU = intensive care unit; PDA = patent ductus arteriosus; VSD = ventricular septal defect.

Operations were performed on COVID-19-positive patients in the post-operative period; VSD closure (n:2), end-to-end repair due to aortic coarctation (n:1), ASD–VSD closure (n:1), VSD–PDA closure (n:1), Norwood stage 3 (Fontan) (n:1), aortic ridge resection (n:1), ASD closure (n:1), cone-type repair due to Ebstein's anomaly (n:1), arch reconstruction (n:1), total correlation was performed due to Tetralogy of Fallot (n:1) (Table 1). All operated patients were asymptomatic and RT-PCR COVID-19 tests of the patients taken in the preoperative period were negative.

Preoperative White Blood Cell values ranged from 5.63 to 11.87 10^3/mcL with a mean of 8.62 ± 2.04103/mcL. Preoperative C-reactive protein values ranged from 0.29 to 5.93 mg/dL with a mean of 2.28 ± 2.05 mg/dL. Preoperative Neutrophil values ranged from 2.24 to 4.83 10^3/mcL with a mean of 3.12 ± 0.97 10^3/mcL. Preoperative Lymphocyte values ranged from 1.29 to 7.37 10^3/mcL with a mean of 4.19 ± 2.18 10^3/mcL. Preoperative Monocyte values ranged from 0.64 to 1.74 10^3/mcL with a mean of 1.01 ± 0.38 10^3/mcL. Preoperative Eosinophil values ranged from 0.07 to 0.65 10^3/mcL with a mean of 0.22 ± 0.16 10^3/mcL. Preoperative Basophil values ranged from 0.02 to 0.13 10^3/mcL with a mean of 0.06 ± 0.03103/mcL (Table 2).

The WBC value of 2 patients out of 11 patients was slightly above the normal range in the preoperative period (ratio 18.18%). The CRP value of 4 patients out of 11 patients was slightly above the normal range in the preoperative period (36.36%). The NEU ratio of 7 patients out of 11 patients was slightly below the normal range in the preoperative period (ratio 63.63%). The LYM rate of 3 patients out of 11 patients was slightly above the normal range in the preoperative period (ratio 27.7%). The MON ratio of 10 patients out of 11 patients was slightly above the normal range in the preoperative period (ratio 90.90%).

The LYM value of 6 patients out of 11 patients was slightly above the normal range in the preoperative period (ratio 54.54%). The MON value of 9 patients out of 11 patients was slightly above the normal range in the preoperative period (ratio 81.81%). The EOS value of 1 patient out of 11 patients was slightly above the normal range in the preoperative period (ratio 9.09%) (Figs. 3 and 4, Table 3).

Table 2. Preoperative laboratory tests.

	Preoperative laboratory tests			
	Minimum	Maximum	Mean	Std. deviation
WBC (10^3/mcL)	5.63	11.87	8.62	2.04
CRP (mg/dL)	0.29	5.93	2.28	2.05
NEU (10^3/mcL)	2.24	4.83	3.12	0.97
LYM (10^3/mcL)	1.29	7.37	4.19	2.18
MON (10^3/mcL)	0.64	1.74	1.01	0.38
EOS (10^3/mcL)	0.07	0.65	0.22	0.17
BAS (10^3/mcL)	0.02	0.13	0.06	0.03

Discussion

There are still many unknowns about the COVID-19 virus we met over a year ago. COVID-19 continues to confuse clinicians both due to its mutations and its different course in each patient. We retrospectively examined the leukocyte profile of 11 patients with asymptomatic and PCR negative post-operative COVID-19 RT-PCR positivity in the preoperative period in our study.

Song et al, stated in their study on COVID-19, influenza, and bacterial pneumonia that laboratory tests for differential diagnosis of COVID-19 could be correlated with the clinic and could help in the diagnosis of COVID-19.[7] It should be kept in mind that

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Table 3. Preoperative hemogram parameters of patients.

	WBC	CRP	NEU	LYM	MON	EOS	BAS	NEU	LYM	MON	EOS	BAS
Range	4.3–10.3	0–3.4	40–74	10–58.5	4–9	0.9–6	0–1.5	2.1–6.1	0.6–4.1	0.3–0.8	0–0.5	0–0.2
Unit	10^3/mcL	mg/dL	%	%	%	%	%	10^3/mcL	10^3/mcL	10^3/mcL	10^3/mcL	10^3/mcL
1	9.88	**5.93***	**23.7****	**65.2***	8.7	1.9	0.5	2.34	**6.44***	**0.86***	0.19	0.05
2	7.71	0.78	49	35	**10.8***	4.7	0.5	3.78	2.7	**0.83***	0.36	0.04
3	9.14	0.79	**28.2****	**59***	**9.6***	1.8	1.4	2.58	**5.39***	**0.88***	0.16	0.13
4	**11.76***	0.53	**19.5****	**62.7***	**14.8***	2.6	0.4	2.3	**7.37***	**1.74***	0.3	0.05
5	8.77	0.63	**28****	52.7	**11.1***	**7.4***	0.8	2.46	**4.62***	**0.97***	**0.65***	0.07
6	8.48	0.29	54.5	33.8	**9.8***	1.1	0.8	4.62	2.87	**0.83***	0.09	0.07
7	5.92	**4.71***	64.7	22.8	**10.8***	1.4	0.3	3.83	1.35	0.64	0.08	0.02
8	5.63	2.21	**39.7****	44.8	**11.4***	3	1.1	2.24	2.52	0.64	0.17	0.06
9	8.7	**3.97***	**26.8****	53.8	**15.2***	3.5	0.7	2.3	**4.7***	**1.3***	0.3	0.1
10	7.03	**4.33***	68.7	18.3	**11.7***	1	0.3	4.83	1.29	**0.82***	0.07	0.02
11	**11.87***	1.01	**25.8****	58.4	**14***	1.2	0.6	3.07	**6.93***	**1.66***	0.14	0.07

BAS = Basophil; CRP = C-reactive protein; EOS = Eosinophil; LYM = Lymphocyte; MON = Monocyte; NEU -= Neutrophil; WBC = White blood cell.
*Above normal.
**Below normal.

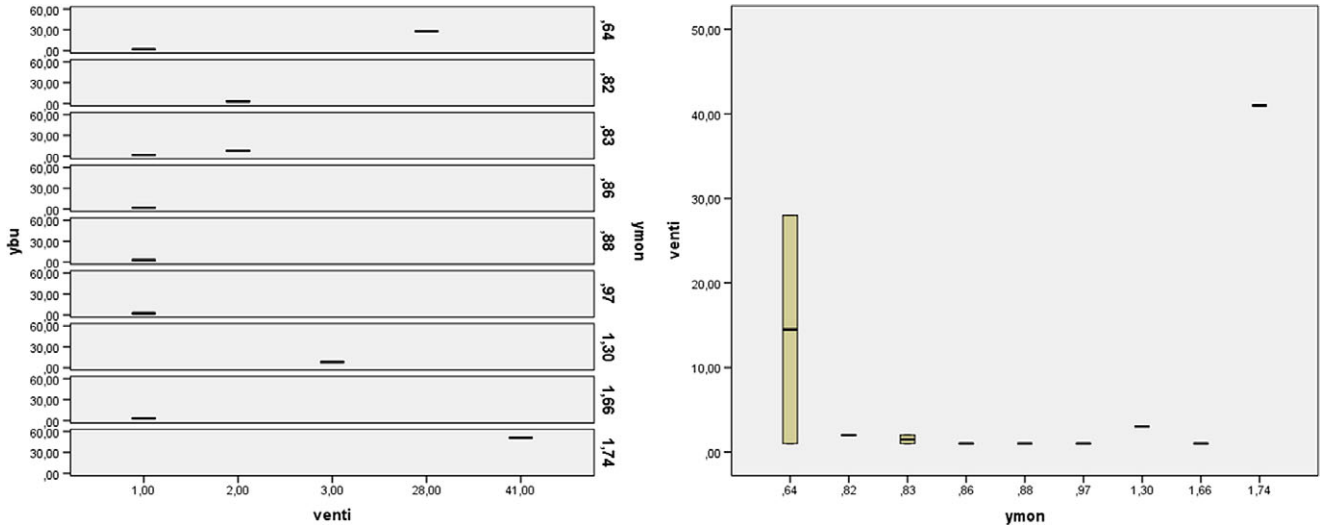

Figure 3. ICU, ventilator, and monocyte value box plots graph.

laboratory tests may lead to diagnosis even if PCR is negative in asymptomatic patients.

Xia et al did not recommend thoracic CT as an early diagnosis tool in the paediatric patient group because it did not contribute adequately to the diagnosis in their study. RT-PCR was reported to be more valuable for the diagnosis of COVID-19 in the paediatric population and they argued in this study that CT should be preferred only in patients with lung involvement due to its possible harms.[8] We made preoperative preparations according to the results of routine lung film, COVID-19 PCR tests, physical examination, and acute phase reactants during the preoperative preparation in our clinic. A routine CT scan was not performed and CT was requested only for one patient with lung involvement.

Porto et al found that leukocyte counts below 5400/μL, relative monocytosis (>9%), eosinopenia and elevation in CRP, anosmia/hyposmia, and body pain within the first 7 days after the onset of fever were predictors of COVID-19 in their study investigating which laboratory results were significant to support the diagnosis in patients with COVID-19 RT-PCR positive as well as situations where COVID-19 RT-PCR was not possible.[9] We found that 10 (90.90%) of these 11 asymptomatic patients had relative monocytosis when we examined preoperative hemogram values in our study. The other patient was very close to the upper limit with 8.7%.

Zhao et al reported in their study on adults that COVID-19 caused a strong natural inflammatory immune response and decreased lymphocytes such as other respiratory viruses after its development from infection.[10] We could not detect clinic signs and lymphopenia in the preoperative paediatric patient group, which we thought to be in the incubation period or early asymptomatic stage.

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Lei et al found that macrophage and neutrophil infiltration of infected lungs increased proinflammatory cytokines and chemokines levels and there was a relationship between high inflammatory cytokine levels and the severity of the disease in their study on adult patients in the incubation period in the preoperative period.[11] We did not find a significant preoperative increase in CRP values due to the asymptomatic and mild course of COVID-19 virus in the paediatric population unlike the adult group in our study. We believe that preoperative clinical and laboratory values of this less affected population may be misleading, even if mortality and morbidity independent of post-operative surgery are more favourable compared to adults. We would also like to note that post-operative elevation of CRP values is not only due to infection and may also increase due to operation.

Spoulou et al found that the symptoms were very mild and neutropenia and monocytosis were present in hemogram in their COVID-19 study in the infant and paediatric population. Lymphopenia has not been seen in any patient. They attributed this to high thymic output and lower cytokine reaction of immature monocytes in the early stages of life.[6] Similarly, lymphopenia was not detected in patients undergoing preoperative incubation and monocytosis was observed instead in our study.

Götzinger et al reported in their study on a high number of paediatric populations that SARS-CoV was mild in the paediatric population, including infants, and rarely required intensive care and mechanical ventilation.[12] One out of 11 patients died and 1 patient needed prolonged ventilation in our study. We believe that the course of non-complex cardiac patients with COVID-19 positivity is thought to be similar to the uninfected population and that COVID-19 and surgical planning schemes, which are increasingly involved in our daily lives, should be reviewed with increasing knowledge and experience.

Guo et al stated in their study that PCR tests may be false negativity due to inadequacies due to material intake, failure to process and send properly, changing the genetic structure as a result of viral mutation, and periodically changing virus scattering of the disease.[13] It is inevitable to increase the rate of false negativity when the difficulty of PCR test intake and patient incompatibility are added in the paediatric population in addition to these causes of false negativity in the adult group. We also take preoperative PCR tests from the parents who are close to the possible infection and who accompany them in the hospital while performing PCR sampling in the paediatric group.

Conclusion

We think that evaluating the leukocyte profile combined with RT-PCR will give more accurate results in the diagnosis of incubation period and false RT-PCR negative patients. In addition, we believe that the algorithms for non-complex paediatric cardiac surgery procedures and timing in the paediatric population with a better course of COVID-19 disease can be revised in light of new information and approached more moderately.

Limitation. This is a retrospective and single-centre study. Larger population studies are needed in this patient group.

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Conflict of interests. None.

Institutional review board approval or waiver. The study protocol was approved by hospital management. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient consent statement. Consent was not obtained and waived.

Data availability statement. Data sharing is not applicable for this article as no new data were created or analysed in this study.

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