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Original article

Evaluation of stool and urine parameters correlation to CRP and D-dimer in COVID-19 infected adults and their contact children

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ABSTRACT

Aim: Aim is to depict suggestive urine and stool parameters in asymptomatic suspected contact children living with COVID-19 infected adults. These parameters will facilitate identifying children who deserve the confirmatory diagnosis of COVID-19 by PCR test. **Methods:** Study was conducted in the National Hepatology and Tropical Medicine Research institute (NHTMRI) Cairo, Egypt. It included 66 mild COVID-19 adult patients (group1) and their 82 asymptomatic contact children (group 2). **Results:** In group 1, both C reactive protein (CRP) and D-dimer levels were significantly high. C reactive protein was significantly positively correlated with urinary microalbumin> 30, albumin/ creatinine ratio and urine pus >10 cells / HPF and significantly negatively correlated with vitamin C. D-dimer was significantly negatively correlated with vitamin C. In group 2, CRP and D-dimer were significantly negatively correlated with urine specific gravity (SG), urinary vitamin C. CRP was significantly negatively correlated with stool pus > 10 cells/ HPF, while D-dimer was significantly positively correlated with stool occult blood. Receiver Operating Curve (ROC) analysis revealed that urine SG showed the highest area under the curve (AUC); 0.859, 0.96, sensitivity of 100%, 100% and specificity of 71.8%, 77.8% with reference to D-dimer and CRP; respectively. **Conclusions**: In contact children of adult COVID-19 proved infection, urine SG, stool occult blood and stool pus > 10 cells/ HPF can be feasible tool for suspected COVID-19 infection, based on its results COVID-19 PCR request can be an imperative option to confirm the diagnosis; particularly in developing countries where detection of COVID -19 by PCR is not readily feasible.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) is the cause of the current pandemic of coronavirus disease 2019 (COVID-19), which has significantly affected all aspects of life; not only the medical but the economic and social aspects as well [1].

One of the main challenges is to identify the suspected COVID-19 cases and confirm the diagnosis as early as possible to ensure proper early

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management and monitor the potential progression. There is an urgent need to have inexpensive easy tools to report, predict and categorize COVID-19 infected cases. Though many laboratory tests are used to diagnose COVID -19 infection, the concomitant use of different diagnostic tests is highly recommended to achieve adequate sensitivity and specificity [2]. Polymerase chain reaction (PCR) assessment remains the gold standard and most commonly recommended test to diagnose COVID-19 [3]. Increased levels of D-dimer and C reactive protein (CRP) are considered to be important associated prognostic biomarkers for COVID-19 infection [4,5].

The incidence of abnormal urine analysis in COVID-19 infection is closely associated with the increased severity and poor prognosis of COVID-19 patients [6]. Severe acute respiratory syndrome coronavirus 2 RNA has also been detected in the feces of adult and pediatric patients up to 12 days after testing negative in respiratory samples [7]. It is also recommended to screen the stool composition as well as to assess the activity of gut microbes [8]. Many authors have been highlighting the importance of urine and stool assessment in COVID-19 cases and emphasized that these simple inexpensive measures are of value; particularly for individuals in underdeveloped countries and remote regions and countries where molecular diagnosis resources are lacking [9].

Persistent shedding of SARS-CoV-2 in stools of infected children raises the possibility that the virus might be transmitted resulting in infection spread causing a major public health burden [10,11].

In many developing countries, the unavailability and high cost of the RT-PCR test limited significantly the screening and diagnosis of COVID-19 among exposed and suspected children. Moreover, that authorities prioritize the screening and diagnosis of COVID-19 infection to the adult population compared to the pediatric population. Therefore, the assessment of urine and stool, as inexpensive, easy and noninvasive diagnostic tools among children are warranted, considering that they did not gain enough attention from researchers. To this end, this study aims to depict the non-invasive urine and stool findings that are correlated to the COVID-19 reliable surrogate parameters; CRP and D-dimer in both adult and children, and assess their possible predictive ability. The performance of these parameters can be recommended in children as a preliminary step prior to requesting the COVID-19 PCR test. This will provide a reliable cost benefit advantage to have a targeted selection of the suspected cases who deserve further confirmation by COVID-19 PCR test.

Materials and Methods

Study type and target population

This study is a prospective randomized observational clinical study conducted in the National Hepatology and Tropical Medicine Research institute (NHTMRI) Cairo, Egypt from March to June 2021.

The study included 2 groups: 66 adult infected COVID-19 patients (group1), confirmed by PCR and classified as mild cases, therefore did not need hospital admission. The other group included 82 children who are living with their parents (group2), but did not yet develop any COVID-19 clinical manifestations. The study, via detailed history and proper thorough medical examination, excluded any adults or children suffering from any other additional comorbid conditions or diseases.

Written, verbal consents were taken from each patient by parents. Each adult patient and his/ her child/children were subjected to the following: questionnaire (name, age, gender, level of education for parents, complaint, fever, cough, body aches), physical examination and laboratory examination:

Samples collection and procedures

Five ml of peripheral venous blood by plane vacutainer tube for assessment of automated quantitative CRP using CRP Reagent Specification commercially available by HEALES; Shenzhen Housing Technology; China.

Five ml of peripheral venous blood by vacutainer tube containing citrate for assessment of automated quantitative D-dimer using D-dimer Reagent Specification commercially available by HEALES; Shenzhen Housing Technology; China.

Fresh stool sample collected in a dry, sterile and labeled container, examined macroscopically, microscopically and for fecal occult blood detection using ACRO BIOTECH kits, USA, KITS.

Fresh urine sample collected in dry, sterile and labelled container, examined macroscopically, microscopically and for biochemical reactions using DIRUI H14-ca kits and DIRUI H-500 automated device.

Statistical methods

Statistical analysis was carried out using SPSS v22.0 IBM statistical package for social science. Categorical data were subjected to descriptive analysis using frequency and percentage, while scale data was described as s mean, standard deviation (SD). Tests for inferential statistics of two groups were chi square test, followed by LSD test. The correlation of nonparametric data was done using Spearman; s rho test. The Receiver operating curve (ROC) was used as predicative tool for

COVID-19 infection with reference to CRP and D-dimer. The significance level was set to p <0.05.

Ethics statement

The study was approved by Ethical Committee of the General Organization for Teaching Hospitals and Institutes (GOTHI), Egypt. Also, written as well as verbal consents were taken from each patient by parent/parents or guardians.

Results

The current study included two groups; the first group comprised of 66 adult patients (34 males and 32 females), with mean age 36.97 ± 5.8 years, with clinical diagnosis of COVID-19 that was confirmed with RT-PCR test. The second group included 82 contact children (44 males and 38 females) who are living with their adult parents in group 1. The average age of those children is 10.45 ± 3.75 years. These contact children did not show any clinical manifestations of COVID- 19 and did not perform the PCR test; They have a potential risk to catch COVID-19 infection Serum CRP and D-dimer, the surrogate markers of COVID-19 infection, were assessed in both groups, as well as a complete urine and stool analysis.

CRP and D-dimer results

Concerning pro-inflammatory diagnostic markers of COVID-19 infection, the CRP level was higher than normal (n.;< 10 mg/dL) in all COVID19 infected adult cases (group1). The mean level was 48 ± 40.2 mg/dL. Though the mean level of the contact children (group 2) was 8.84± 8.5, which indicates near normal level in most of them, only19.5% of this group 2 had their CRP level exceeding 10 mg/dL. In alignment of CRP, the D-dimer (n.;< 0.5 mcg/mL) was higher than normal in all adult cases group1, with a mean level of 1.5± 0.5, while in the contact children group 2 was significantly lower (0.64± 0.5); 40.2 % of the contact children exceeded 0.5 mcg/mL.

Urine findings

Concerning the assessed urinary microscopic findings, as shown in **tables (1)** and **(2)**, 23 of the adult infected cases (34.8%) showed pus cells level > 10 HPF, compared to 16 in the contact children (19.5%). The number of adult patients with significant microscopic epithelial cells higher than the normal level (1-5 /HPF) was 10 (15.15%), compared to 5 children (6%) in the contact children group 2. Both groups had comparable levels of significant bacteria, microscopic ureates and RBC > 10 HPF. The levels of lbumin/ Creatinine ratio > 30 and creatinine > 50 were reported in a significantly higher percentage in the adult cases group1, compared to the contact children group. Concerning the urine specific gravity of 1.015, it was comparable in both groups (53%, 45.12%), while 1.02 was higher in the adults' group (36.4%,23.2%) and 1.025 was higher in the pediatric group (10.61%,31.7%). Concerning the vitamin C and calcium levels in the urine, they were significantly higher in adults, compared to their contact children. The percentage of adults to children was for vitamin C (54.5%, 6%) and calcium (27.3%, 8.5%;).

Stool findings

The stool findings in both groups are presented in **tables (3)** and **(4)**. Stool parasites were significantly high in adult cases as well as contact children group. While the number of infected adults and their contact children having stool pus >10 was significantly high.

CRP and D-dimer level correlation to urine and stool finding

In an attempt to identify non-invasive diagnostic and predictive markers of COVID-19 In adult cases group, as shown in **table (5)**, CRP was significantly positively correlated with microalbumin > 30 (r = 0.234, p= 0.049), albumin/ creatinine ratio (r = 0.176, p= 0.049) and urine pus >10 cells / HPF (r = 0.321, p = 0.009) and significantly negatively correlated with vitamin C (r = -0.358, p = 0.003), while the negative correlation with stool RBC > 10/HPF did not reach significance (r = -0.22, p=0.074). D-dimer in the adult cases group was significantly positively correlated with urine bacteria (r= 0.22, p= 0.03) and stool parasite (r= 0.279, p= 0.023), while the negative correlation with vitamin C did not reach significance (r = - 0.28, p= 0.02). In the contact children group, CRP and D-dimer were significantly negatively correlated with urine specific gravity (r= - 0.312, p= 0.005 and r = -0.272, p=0.014, respectively), and also vitamin C in urine (r= -0.276, p= 0.013 and r =-0.201, p= 0.04; respectively). Moreover, CRP was significantly negatively correlated with stool pus > 10 cells/ HPF (p=0.019), and D-dimer was positively correlated with stool occult blood (p=0.002).

In an attempt to identify urine as a suggestive tool that can be correlated with CRP and D-dimer in possible COVID-19 infection in suspected children, their specificity and sensitivity were analyzed using their ROC. In children group, as shown in **table (6)**, the correlated urine suggestive findings markers with the respective serum D-dimer levels were urine specific gravity, urinary vitamin C and stool occult

blood. The ROC analysis as shown in **figure (1)** revealed that using the urine specific gravity showed the highest area under the curve (AUC); 0.859, sensitivity of 100% and specificity of 71.8%. Using stool occult blood showed a lower AUC of 0.62 and sensitivity of 50% and specificity of 74.4%. **Figure 2** shows that the ROC analysis of urinary markers with the respective serum CRP levels were urine specific gravity, urinary vitamin C and stool pus >10. The ROC analysis revealed that using the urine specific gravity showed the highest area under the curve of 0. 96, sensitivity of 100% and specificity of 77.8%. Using urinary vitamin C showed an AUC of 0.468, sensitivity of 50% and specificity of 69.4%. Moreover, stool analysis revealed an AUC of 0.468 and sensitivity of 60% and specificity of 79.5%.

Table 1. Urine analysis of adult COVID-19 patients (Group 1).

Urine parameters	**Group 1 Adult cases (**number =66)	
	number	%
Microscopic RBCs > 1 *(*n.; 0-10 /HPF]	10	15.15
Microscopic pus > 10 *(*n.; 0-10 /HPF*)*	23	34.8
Microscopic bacteria (n; nil)	6	9.09
Microscopic epithelial cells (n.; 1-5 /HPF)	10	15.15
Microalbumin > 30 (n.; <30 mg/L)	18	27.27
Albumin/ Creatinine ratio > 30) n;< 30*)*	18	27.27
Creatinine > 50 *(*n.; 50 mg/dL*)*	7	10.6
Glucose > 100 mg/dL) n; nil*)*	2	3.03
Urine SG		
< 1.015	35	53.03
1.015-1.02	24	36.36
>1.02	7	10.61
VITC >10) n; <10 mg/dL	36	54.55
Calcium >12 *(*n; <12 mg/dL	18	27.27

Table 2. Urine analysis of the contact children of the adult COVID-19 patients (Group 2).

Urine parameters	**Contact children number =82**	
	number	%
Microscopic RBCs > 1 *(*n.; 0-10 /HPF]	17	20.7
Microscopic pus > 10 *(*n.; 0-10 /HPF*)*	16	19.5
Microscopic bacteria (n; nil)	4	4.88
Microscopic epithelial cells (n.; 1-5 /HPF)	5	6.1
Microalbumin > 30 (n.; <30 mg/L)	13	15.85
Albumin/ Creatinine ratio > 30) n;< 30*)*	12	14.63
Creatinine > 50 *(*n.; 50 mg/dL*)*	1	1.22
Glucose > 100 mg/dL) n; nil*)*	0	0
Urine SG		
< 1.015	37	45.12
1.015-1.02	19	23.17
>1.02	26	31.7
VITC >10) n; <10 mg/dL	5	6.1
Calcium >12 *(*n; <12 mg/dL	7	8.54

Table 3. Stool findings of the adult COVID-19 patients (Group 1).

Stool findings	**Adult cases number = 66**	
	number	%
Stool parasite) n; nil)	2	3.03
Stool pus > 10) n; 0-10 /HPF)	14	21.21
Stool RBCs > 10) n; 0-10 /HPF)	3	4.55
Stool occult blood) n; nil)	14	21.21

Table 4. Stool findings of the contact children of the adult COVID-19 patients (Group 2).

Stool findings	**Contact children number = 82**	
	number	%
Stool parasite) n; nil)	22	26.82
Stool pus > 10) n; 0-10 /HPF)	2	2.44
Stool RBCs > 10) n; 0-10 /HPF)	3	3.66
Stool occult blood) n; nil)	22	26.83

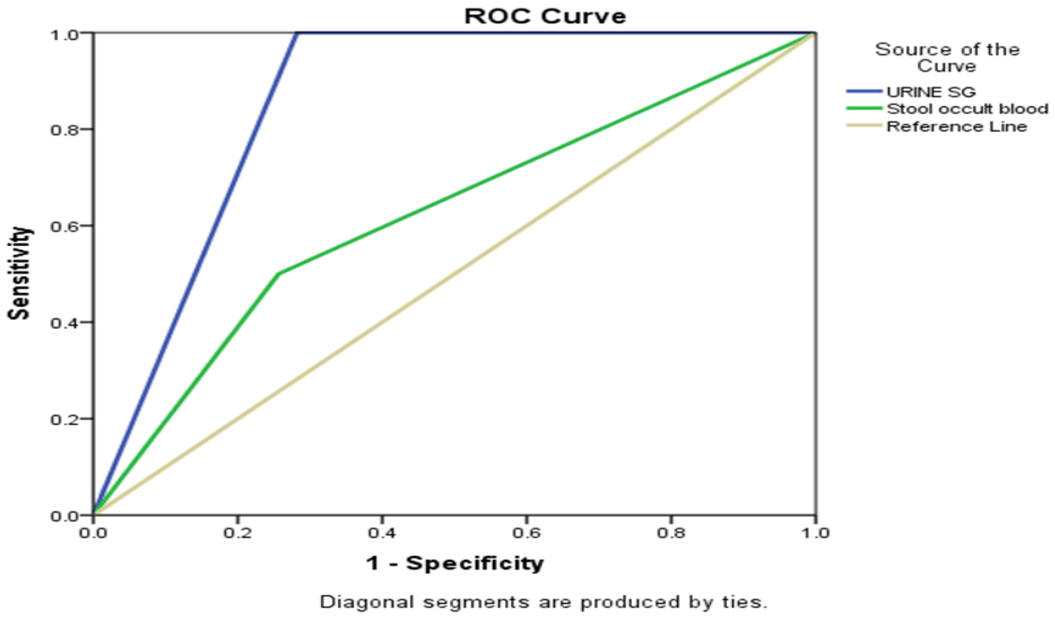
Table 5. Correlation of CRP and D-Dimer levels with the assessed urine and stool parameters in the adult COVID-19 patients.

Adult cases			
Parameters		**CRP**	**D-dimer**
Urine Bacteria	r	-0.044	0.222
	p	0.724	0.03
Urine Microalbumin > 30	r	0.243	0.147
	p	0.049	0.24
Urine Albumin / Creatinine ratio	r	0.243	0.147
	p	0.049	0.24
Urine S.G.	r	0.176	0.01
	p	0.158	0.94
Urine pus > 10 cells/HPF	r	0.321	0.085
	p	0.009	0.496
Urine vitamin C	r	-0.358	-0.285
	p	0.003	0.02
Urine Calcium	r	0.05	0.147
	p	0.69	0.24
Stool parasite	r	0.149	0.279
	p	0.234	0.023
Stool pus > 10 cells/HPF	r	- 0.171	- 0.121
	p	0.169	0.334
Stool RBC > 10	r	-0.222	- 0.203
	p	0.04	0.102
Stool occult blood	r	0.047	- 0.062
	p	0.71	0.619

Table 6. Correlation of CRP and D-Dimer levels with the assessed urine and stool parameters in the contact children of the adult COVID-19 patients.

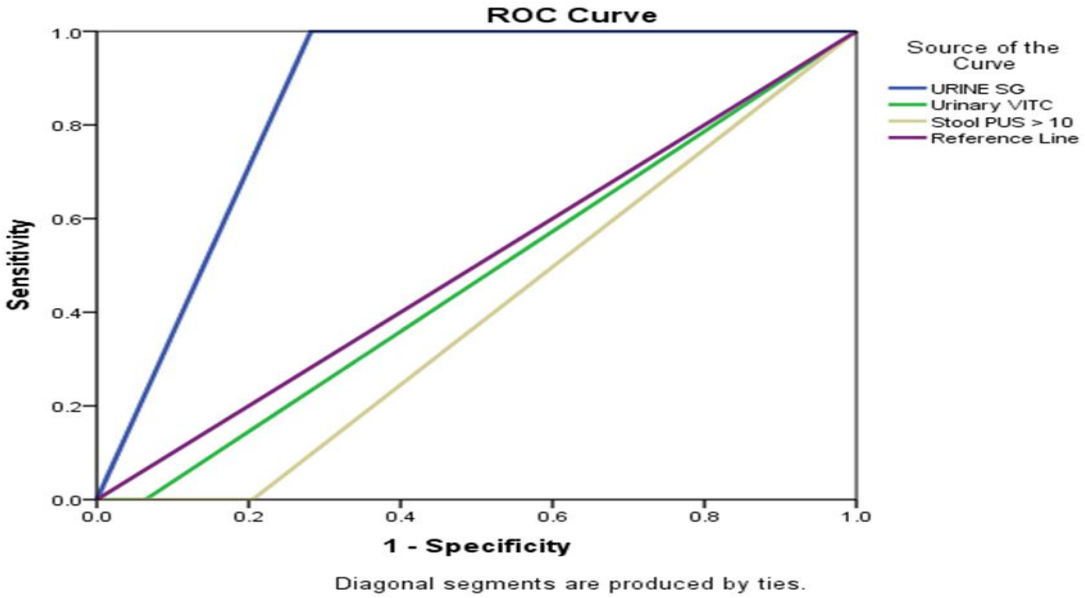
Contact children			
Parameters		**CRP**	**D-dimer**
Urine Bacteria	r	- 0.027	-0.179
	p	0.81	0.11
Urine Microalbumin > 30	r	0.098	0.081
	p	0.38	0.47
Urine Albumin / Creatinine ratio	r	0.06	0.11
	p	0.59	0.32
Urine S.G.	r	- 0.312	- 0.272
	p	0.005	0.014
Urine pus > 10 cells/HPF	r	-0.044	-0.087
	p	0.7	0.44
Urine vitamin C	r	- 0.276	-0.201
	p	0.013	0.04
Urine Calcium	r	- 0.113	- 0.068
	p	0.32	0.55
Stool parasite	r	- 0.116	0.002
	p	0.30	0.99
Stool pus > 10 cells/HPF	r	- 0.261	-0.125
	p	0.019	0.26
Stool RBC > 10	r	- 0.064	- 0.154
	p	0.573	0.168
Stool occult blood	r	0.061	0.345
	p	0.59	0.002

Figure 1. Receiver Operating Curve (ROC); The sensitivity and specificity of urine specific gravity, stool occult blood with reference to D-Dimer in contact children of COVID-19 adult patients.



Diagnostic marker	AUC	Sensitivity	Specificity
D-Dimer	0.97	100 %	97.4 %
Urine Specific Gravity	0.859	100 %	71.8%
Stool occult blood	0.62	50%	74.4%

Figure 2. Receiver Operating Curve (ROC); The sensitivity and specificity of urine specific gravity, urinary Vit C and stool pus>10 with reference to CRP in contact children of COVID-19 adult patients.



Parameter	AUC	Sensitivity	Specificity
CRP	0.98	100 %	98 %
Urine Specific Gravity	0.859	100 %	71.8%
Urinary Vit C	0.468	50%	69.4%
Stool pus >10	0.487	60 %	79.5%

Discussion

Rapid and accurate laboratory diagnosis of COVID-19 infection is the most important preliminary step for its proper management. The RT-PCR test remains the gold standard to confirm COVID-19 infected cases, however it is relatively expensive and not readily available, also time consuming. All these factors limit its routine use especially in the low- and middle-income developing countries [12]. The same challenges apply for the close contact children of the COVID-19 infected parents, in whom the majority would be commonly asymptomatic, constituting a dilemma about the proper approach to deal with those children. The household contacts are at higher risk for COVID- 19 infection, especially from symptomatic cases [13]. The early screening of the asymptomatic infections with COVID-19 among those close contacts children is important so as to be traced and investigated via reliable readily available inexpensive tests in order to decide on further management steps. The urine and stool analysis opens new horizons for predictive testing for COVID-19, an area that has not been thoroughly tested, especially in children who need noninvasive tolerable tools for assessment. Our study showed that both CRP and D-dimer diagnostic tests were higher than normal values in all of the adult cases, while in the contact children group, the values were significantly lower; as 40.2 % and 15% of group 2 exceeded the normal values of CRP and D-dimer, respectively. These findings coincide with the results of **Rostami et al.** [14] who noted that high CRP and D-dimer levels have been reported in the early course of COVID-19 infection. Moreover, **Tan et al.** [15] noticed that CRP marker was found

to be significantly increased in the initial phases of the infection for COVID-19 patients, and has been associated with disease development which could be used as an early predictor for severe COVID-19. The findings of our study are in harmony with another study [16] that showed that CRP and D-dimer levels are correlated with severity of infection with COVID-19 and can be used as predictive biomarkers in adults and children [17] infected with COVID-19, However, the incidence is higher in adults [18] for COVID-19 prognosis and from the early stage of the disease emphasizing that it can also be useful in controlling and management of the disease. Our study showed that 15.15 % of adult cases showed hematuria, microscopic RBCs > 10 /HPF, these finding is in alignment with that of **Sundaram et al.** [19] who reported significant hematuria in 17.3% of cases and with **Allemailem et al.** [20] who reported hematuria in 22.3% of infected patients. In our study, 23 adult cases (34.8%) showed pus cells > 10 HPF coinciding with the study by **Allemailem et al.** [20] who found that 33.7% of the studied cases had pus in their urine. Another study showed lower percentage of pyuria (8.2%) in COVID-19 infected patients [19]. In the current study, there were 16 contact children (19.5%) with urine pus cells > 10 HPF, while only 5 children (6%) with urine pus cells > 10 HPF (p= 0.05). In our study urinary microscopic bacteria were found in 9 % of our adult cases compared to another study that reported bacteria in 19.9% of the studied cases [21]. Our contact children cohort showed lower value; only 4 children (4.88%) with urine bacteria. The number of adult patients with significant microscopic epithelial cells, who were higher than the normal level (1-5 /HPF), was 10 (15.15%), which may indicate upper urinary tract infection [22]. Our contact children cohort showed lower value only 5 children (6.1%) with epithelial cells> 5/HPF. Our study showed that 18 adult cases have proteinuria (27.27 %). This percentage is lower than that reported by **Sundaram et al.** [19] that showed proteinuria in 58.2 % of patients and also lower than that by **Allemailem et al.** [20] who found proteinuria in 53.9% of patients. These findings can be explained that the in our study the cases are mild cases and the kidney affection was mild; while both of the above-mentioned studies involved hospitalized moderate to severe cases. These findings are also supported by the study of **Gabarre et al.** [23] who suggested that two phenotypes of proteinuria have been identified in COVID-infection; the first when proteinuria is of small amount; as in our study, probably indicating tubular injury. The second phenotype is evident when proteinuria is abundant suggesting glomerular impairment. Furthermore, another study [24] suggested that proteinuria in cases of COVID-19 without acute kidney injuries is often mild and transient. **Ouahmi et al.** [25] stated that proteinuria is an easily measurable marker to assess the severity of COVID-19 infection and to predict outcome as well. In the current study, a small number of the contact children had significant proteinuria (13, 15.85%). Our study showed also that the 18 adult cases with high proteinuria showed also elevated albumin/creatinine ratio > 30 mg/mmol and this may suggest tissue damage at both the glomerular and tubular parts of the kidneys, as suggested by **Luther et al.** [26] who found the same high ratio in 17% of the patients of their study. Our results showed 12 contact children (14.63%) with elevated albumin/ creatinine ratio > 30 mg/mmol, but significantly lower than adult cases group. Concerning elevated urinary creatinine, our study showed 7adult cases (10.6%) with elevated creatinine > 50 mg/dL but only 1 contact child (1.22%) with elevated creatinine level > 50 mg/dL. In a study by **Liu et al.** [27], glucose was detected in the urine of severe and critical cases higher than those in the moderate group ($p < 0.01$ and $p < 0.05$, respectively). Contradictory to the previous finding, in our mildly infected patients, urine glucose was detected in only 2 of our adult cases and was not detected at all in any of the contact children. Urine specific gravity (SG) was low in the majority of our adult study cases. Only 7 cases (10.61%) showed high urine SG more than 1.02 and this coincides with the findings of **Liu et al.** [27] who found that the urine SG value was lower in patients than in healthy controls. Other authors correlated high urine specific gravity with imminent acute kidney injury [28]. The urine SG of our adult cases was significantly higher than cohort contact children. Although there is as yet no direct evidence indicating that vitamin C is beneficial specifically against COVID-19, but many authors [29] suggested benefits of vitamin C intake and that it should be considered for patients. The prevalence of this concept led to an increase in the intake of vitamin C among patients in exaggerated quantities. However, other authors [30] stated that significant amounts of vitamin C intake will result in excessive vitamin C excretion in urine and can increase the

risk of kidney stones and elevate uric acid and oxalate because it would acidify the urine. In our study, high level of vitamin C in urine was observed in many adult cases (54.55%) that may indicate high dose intake of vitamin C. This is significantly higher than our contact children group (6.1%). In our study excessive calcium excretion in urine was observed in 18 adult cases (27.27%), which is significantly higher than our contact children group (8.54 %). It is worth to highlight the importance of assessment of calcium excretion in urine in COVID 19 cases as many of them take vitamin D due to the recommendations of its beneficial role for COVID 19 management [31]. However excessive vitamin D intake is associated with hypercalciuria [32], therefore the rational intake of vitamin D is advised to avoid potential adverse consequences [33]. Gastrointestinal manifestations are present in many of COVID-19 infected cases [34]. These manifestations include anorexia, diarrhea, nausea and vomiting and have been reported in both adults and children [35]. Dysentery can be the only manifestation of COVID- 19 infection [36]. Some of these manifestations may be associated with intestinal parasitic infection as well. In our study, we found that only 2 of our adult cases (3.03%) had intestinal parasites compared with 22 contact children (26.83%). This significant result highlights the importance of searching for intestinal parasite among suspected COVID-19 infected children so as not to be mistaken with these similar manifestations. In our cohort study, pus cells were detected in 14 of the adult cases (21.21; this was in a significant contrast to the findings of the contact children in whom only 2 children (2.44%) showed pus in their stool. Our findings coincide with that **of Yeoh et al.** [37] who found that gut bacteria were depleted inpatients with COVID-19 and their gut microbiome composition was significantly changed compared with non-COVID-19 individuals. They suggest that depletion of immunomodulatory gut microorganisms contributes to severe COVID-19 disease. In our study, occult blood was detected in the stool of 14 adult cases (21.21%) higher than other study [38] that occult blood was detected in 6.8% of patients. The occult blood was detected in 22 of our contact children cohort (26. 83%). Our results revealed that in the adult cases positive significant correlation of CRP with urine microalbumin > 30, urine albumin / creatinine ratio, urine pus> 10 and stool RBCs > 10 /HPF. We also found in the adult cases positive significant correlation of D-dimer with urine bacteria and stool parasites were stated. Our study showed in the contact children, significant negative correlation of CRP with urine specific gravity, and stool RBCs >10 /HPF were reported. We also found significant negative correlation of D-dimer with urine specific gravity and stool occult blood. Urine vitamin C is the only parameter that showed significant negative correlation with both CRP and D-dimer levels within adult cases and their contact children group.

In an attempt to identify the predictive urine parameters that are correlated with CRP and D-dimer in suspected COVID-19 children, the performed ROC analyses revealed that using the urine SG showed the highest area under the curve (AUC); 0.859, sensitivity of 100% and specificity of 71.8%, relative to D-dimer and AUC of 0.96, sensitivity of 100% and specificity of 77.8% relative to CRP. This indicates that it can be used alongside with stool pus and occult blood assessment in the prediction of suspected pediatric COVID-19 cases. Similar findings were reported by **Liu et al.** [27] who tested the utility of urine occult blood and specific gravity in COVID-19 infection severity.

Conclusion

In children suspected of COVID-19 infection, the utility of urine and stool analyses are cheaper, more convenient, and rapid than blood laboratory assessments and RT-PCR testing. Our results suggest that urine SG and stool pus > 10 cells/ HPF can serve as a feasible predictive tool for suspected COVID-19 infection in children, who are in direct contact with their positively infected parents; based on its results COVID 19 PCR request can be an imperative option to confirm the diagnosis; particularly in developing countries where detection of COVID -19 by PCR is not readily available.

Limitations of the study

The authors would like to declare the limitation of the current study. The first limitation lies in unavailability of the COVID-19 viral load in the adult cases stool or urine specimens. Therefore, we were unable to link the virus load to the results of urine and stool assessment. The second limitation is that some adult cases who showed high vitamin C level in the urine may have taken frequent doses of vitamin C, which may have affected the vitamin C level; so, determination of the dose of oral vitamin C intake has to be determined so that it can be correlated with urine vit C level.

The third limitation lies in the necessity to recruit a larger sample size to allow higher level of statistical significance. It is also recommended to expand the studied cohort to include moderate and severe cases to assess noninvasive diagnostic markers that can be used for children.Also adult and pediatric control groups can be added.

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Conflict of interest: None.

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