

RESEARCH ARTICLE

A STUDY OF SOME BLOOD PARAMETERS AMONG DENGUE PATIENTS IN LAHJ/ YEMEN

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Abstract

The present study was carried out to evaluate the effect of dengue fever on some hematological and biochemical parameters on patients, whose were infected with dengue virus at AL-Jamaheer Medical Center\ Lahj from July to September 2018.

One hundred and three cases have been tested, among them 52.4% were males and 47.6% were females, the age ranged from a year to 60 years old.

The tests included the evaluation of complete blood count (CBC), aminotransferase levels, glutamic-oxaloacetic transaminase (GOT), and glutamate pyruvate transaminase (GPT), in addition to serum Urea, and creatinine levels.

Hematological tests revealed that approximately 56.3 % of cases showed a decrease in white blood cell (WBC) count with about 4000/ μ l, 19.4% cases with values between 2000 -3000/ μ l and 2000 / μ l in 15.5 % cases, whereas 21.4% cases were with a range between 3000-4000/ μ l.

Platelet counts (PLT) were decreased to <150000/ μ l in 29.2% of cases and were about 50,000- 100,000/ μ l in 13.6% of cases, while showed around 50000/ μ l in 3.9% of cases.

As for the biochemical tests, liver function tests (L.F.T.) showed that an increase was observed in SGOT and SGPT of 42.7 % and 34 % of cases, respectively.

Kidney function tests showed elevated serum urea and creatinine in 2.91% and 5.83% cases, respectively.

In conclusion, one of the predictive markers of dengue fever is a decrease in the number of white blood cells and platelets. In contrast, it raised the levels of amine transporters (SGOT) and (SGPT), Therefore, monitoring these indicators is useful in diagnosing dengue fever in order to provide good health care to patients.

Keywords: Dengue fever, Hematological and Biochemical profile.

Introduction:

Dengue fever aka Aden fever [1], or as well known 'abou-ndefu' of the Hadramaut Arabs [2]. Dengue fever is currently one of the most important human viral mosquito-borne infection of public health with millions of infections each year [3]. The main dengue vector is the female of the *Aedes aegypti* mosquito as well as *Aedes Albopictus* [4, 5, 6].

The dengue virus (DENV) belongs to flavivirus and it has four serotypes of (DEN - 1-4). [4, 5, 7, 8]. All 4

serotypes have diffused in all tropical and subtropical regions of the world. They are antigenically closely related, but whereas infection with one serotype produces lifelong immunity to that serotype, immunity to other serotypes lasts only a few months. [3, 9, 10]. and hence a person may be infected up to four times [7].

The virus encodes for seven non-structural (NS) proteins between these a (NS1) use as a diagnostic antigen in early phases of the disease.

Dengue has an incubation period of 3-14 days while viral replication takes place in target dendritic cells.

commonly, the recovery is completed by 7–10 days [3]. Associated symptoms are headache, retro-orbital pain, nausea, vomiting, abdominal pain, maculopapular confluent rash, severe myalgias and arthralgias especially of the knees and shoulders [1, 7]. And causes 4 spectra of illness which are an asymptomatic phase, acute febrile illness, classic Dengue fever (DF), Dengue Hemorrhagic Fever (DHF) which includes Dengue Shock Syndrome (DSS) [5, 10,11].

One of the target organs for dengue is the liver, and clinical manifestations of hepatic dysfunction can occur during this illness [12].

Elevated aminotransferase is considered one of the features of hepatic involvement during dengue virus infection in these patients.

Transaminase derangements are typically mild and self-sustaining or maybe correlated with more extreme symptoms as resulting from multifactorial disorders in sometimes, such as the use of hepatotoxic medications, as well as the direct aggression by the dengue virus [13].

Dengue viral infection has been recognized as one of the world's biggest emerging epidemic. also, it is considered a major global health threat by the World Health Organization [10, 14].

In Yemen, the breakdown of Yemen's health system, inadequate water and hygiene conditions in the most affected areas, as well as the continuing complicated and protracted war, with restricted access to humanitarian assistance to the most vulnerable and affected populations led to an increase of the incidence of infectious diseases, with an upsurge in outbreaks of dengue. Also, the clinical presentations of dengue infection may mimic other infections, as well as serology testes for definite diagnosis is costly and inaccessible in many hospitals in a developing country like Yemen [15].

We sought to identify the effect of dengue fever on some of the hematologic and biochemical parameters in dengue e patients. And This appears to be the first study that has investigated which effect of dengue fever on some of the hematologic and biochemical parameters in this district. However, there has been very limited research conducted that has studied only two of those blood parameters (white blood cells and platelets).[16]

Material and Method:

We performed a study of all cases admitted to Al-Jamaheer Medical Center from July to September 2018, of 103 patients, which include both males and females and their ages ranged from 1 to 60 years. All the studied cases were selected based on continuous high fever lasting 2 to 7 days and were positive for Dengue Serologic Rapid Test (Cassette).

Sample Collection:

5 ml blood were collected from the patients, 2 ml was taken in a separate test tube containing ethylene di-amino

tetra acetic acid (EDTA) tube and used for estimation of complete blood count (CBC) by automated analyzer Sysmex-xs500i, Germany (3-part differential) according to manufacturers' instructions. The remain 3 ml of blood was allowed the blood to clot in another tube at room temperature for 15-30 minutes, then was centrifuged at 2000 x g for 10 minutes. The supernatant serum was used for biochemical and Dengue Serologic tests.

The biochemical tests were applied by using an automated ChemWell 2910 analyzer (Awareness Technology, Inc., Palm City, FL, USA) with Open Reagent System for Working with liquid Reagents according to manufacturers' instructions.

Serological tests for dengue were diagnosed by using Dengue Ag Rapid Test-Cassette (CTK Biotech, Inc., USA) according to manufacturers' instructions.

For Statistical analysis: Data were analyzed by the SPSS 24 statistical program. Qualitative variables were Presenting as frequencies, percentages, and charts and tested by One-Way ANOVA. Quantitative variables were presented as mean and standard deviation. Statistical analysis was conducted with 95% confidence limits, and a P-value of <0.05 was considered statistically significant.

Ethical Consideration:

The study was performed to achieve a health benefit to the community and to improve the health care of the patients in the medical center and hospitals in general, after taking written consent from the high authority of the medical center and consents be taken from all participants after they had been informed that participation is voluntary and that they can refuse this without starting any reason. All information is confidential, and the results that were used in this study did not mention the names of the patients.

Result and Discussion:

The data of the CBC test as shown in table (1), it revealed that about 56.2% of patients had leucopenia from a total of 103 studied cases. Among them we found neutropenia in 32% of patients, lymphopenia occurred in 39.8% and 86.4% of patients had monocytosis, whereas eosinophil was decreased by 92.2%. The thrombocytopenia was observed in 29.1% of studied cases.

The decrease in leukocyte count of patients who have dengue is mainly due to a decrease in granulocytes such as neutrophils and lymphocytes [17, 18, 19, 20]. Leukopenia often with lymphopenia, is observed near the end of the febrile phase of illness. Lymphocytosis commonly develops before defervescence or shock [21]. Also its a considered common finding for predicting the degree of dengue infection [22].

The absolute monocyte count was significantly increased in secondary dengue infections compared to primary infections [23]. The eosinophil was decreased due in response to inflammation during the acute phase [24,25].

Table (1): Various Hematological parameters in dengue patients.

Parameter	WBC	NEUT	LYMPH	MONO	EO	BASO	PLT
Range	(4-10) ×10 ³ /uL	40-70%	20-45%	2-10%	2-6%	0.0-1.0%	(150-450) ×10 ³ /uL
Number	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Decreased↓	58(56.2%)	33(32 %)	41(39.8%)	0(0%)	95(92.2%)	0(0%)	30(29.1%)
Normal	40(38.8%)	47(45.6%)	37(35.9%)	14(13.6%)	8(7.77%)	96(93.2%)	72(69.9%)
Increased↑	5(4.9%)	23(22.3%)	25(24.3%)	89(86.4%)	0(0%)	7(6.8%)	1(1%)

NEUT= neutrophils, LYMPH= lymphocytes, MONO= monocytes, EO= Eosinophils, BASO= basophils.

As shown in our findings, Leukopenia was more prevalent in patients aged 11-30 years. This result is in agreement with the previous study, where they published, that leukopenia was more prevalent in patients aged 15 years or older by [12, 21, 26].

The mechanism for lower leukocytes may be as a result of suppression of WBC production in bone marrow by the dengue virus during the disease [27].

The result showed thrombocytopenia was more common among the elderly age group (more than 51 years). These findings are in line with the previous study by [12]. Another study showed thrombocytopenia was prevalent in old age groups such as 61-70 years and 71-80 years, respectively as previously reported [28].

Thrombocytopenia may be a reason for developing an acute immune response [29]. The mechanism of DF thrombocytopenia occurs as a result of the direct invasion of megakaryocytes by viruses, leading to increased platelet damage or increased platelet antibodies [21, 28].

Table (2): Comparison between the mean of WBC and PLT with age groups

Parameter		WBC	PLT
Rang		(4-10) ×10 ³ /uL	(150-450) ×10 ³ /uL
Group	N (%)	Mean± SD	Mean ±SD
≤ 10	13 (12.6%)	5.01±2.47	195.15±103.3
11 – 20	34 (33%)	↓3.95±2.00	200.97*±77.2
21 – 30	26 (25.2%)	↓3.97±2.44	175.54±76.07
31 – 40	16 (15.5%)	4.61±3.53	159.25±67.38
41 – 50	10 (9.7%)	4.36±2.12	173.90±95.60
≥ 51+	4 (3.9%)	4.02±2.74	↓113.50±49.62
Male	54(52.4%)	4.06±2.44	159.02±75.53
Female	49(47.6%)	4.42 ±2.49	205.88±80.63
Total	103(100%)	4.23±2.46	181.31± 81.20

Values are presented as mean ± standard deviation. * = a significant difference from the total average for each parameter (P<0.05).

Comparison between Mean of the differential white blood cells count in the different of groups aged and for each parameter table (3), we found neutropenia common in the age group (11-20 years) which was low than normal, while neutrocytosis was in group age for more than 51 years. With no statistically significant differences in the mean values of neutrophil for each

group aged and neutrophil (p>0.05). The mean neutrophil for males and females were within normal limits.

Lymphocytosis was prevalent only in age groups (≥51 years), with no statistically significant differences in the mean values of lymphocyte for each group aged and lymphocyte (p>0.05).

Also, our findings showed that monocytosis was prevalent in all aged groups, and we did not notice significant differences in the mean values of monocytes for each group aged and monocytes (p>0.05).

We observed that all aged groups had eosinopenia, where the mean of eosinophils for each group was lower than normal limits. Also, we noticed a significant difference (p<0.05) only between the mean of eosinophil in the age group (11-20 yrs.) with eosinophil.

According to our data, we observed the means of basophils for age groups were within normal limits. We also noted a significant difference between the mean of basophils for groups aged (31-40yrs) with Basophils.

Kalayanarooj et al, [30] reported that neutrophils were significantly lower in children with early dengue infection compared to other fevers. Hence, these parameters are considered as markers for early diagnosis and follow-up of dengue infection.

In our study, the mean values for lymphocytes were within the normal range except group aged (more than 51 yrs.) which was high than the normal range. Although they were predicted to increase during many viral infections. This result is in line with a study by Ralapanawa et al., [31] who noticed that mean values for lymphocytes were within the normal range.

In our results, monocytosis was a common finding in all cases all aged groups. Although previous a study found that the raise to absolute monocyte count, at secondary dengue infection during the defervescence phase of dengue illness in individuals aged 15 years and older $0.71 \pm 0.15 (x10^9)$ compared to those experiencing primary dengue infection. Replication of dengue virus has been primarily observed in monocytes [22].

According to the means of eosinophils, we observed that all aged groups had eosinopenia. The reason for the decrease of eosinophilic levels in the acute phase due to the response to the inflammatory process, the levels then returning to baseline, and increasing in the convalescence phase [17, 23, 24].

Table (3): Comparison between the mean of the differential white blood cells count with age groups of dengue patients.

parameter		NEUT	LYMPH	MONO	EO	BASO
Rang		40-70%	20-45%	2-10%	2-6%	0.0-1.0%
Group	N (%)	Mean± SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
≤ 10	13 (12.6%)	42.85±20.62	36.92±12.85	↑17.73± 6.27	↓0.56± 0.39	0.29±0.21
11 – 20	34 (33%)	↓39.50±21.39	31.00±13.0	↑21.50± 7.84	↓1.08*±0.90	0.46± 0.32
21 – 30	26 (25.2%)	45.38±22.31	38.46±18.6	↑16.18± 6.23	↓0.90± 0.57	0.37± 0.24
31 – 40	16 (15.5%)	56.00±33.72	41.19±18.2	↑22.25± 9.98	↓0.69± 0.51	0.57*±0.35
41 – 50	10 (9.7%)	41.50±18.23	39.90±19.0	↑26.32± 9.65	↓1.12± 0.94	0.48± 0.31
≥ 51+	4 (3.9%)	↑76.50±14.84	↑57.75±5.85	↑32.70±21.13	↓0.75± 0.33	0.48±0.43
Male	54(52.4%)	49.83±22.52	32.30±20.71	16.05 ±7.29	0.91±0.90	0.48±0.27
Female	49(47.6%)	52.41±20.76	30.00±19.96	16.88±5.26	0.86±1.22	0.39±0.38
Total	103(100%)	45.60±24.34	37.12±16.54	20.70±9.26	0.89± 0.72	0.44± 0.30

Values are presented as mean ± standard deviation. * = a significant difference from the total average for each parameter (P<0.05).

As shown in table (4), our data revealed that the most common hematological abnormality was leucopenia in 58 (56.3 %) patients (total leucocyte count < 4,000 /µl) followed by thrombocytopenia (platelet count less than 1,00,000/µl) in 18 (17.5%) patients. However, we noticed that among studied 103 cases, in 16 (15.5%) cases had WBC count less than (2000 /µl), 20 (19.4%) had WBC count (2000- 3000/µl), 22 (21.4%) cases had WBC count (3000- 4000/ µl), 16 (15.5%) cases had

WBC count (4000- 5000 / µl) and 29 (28.2%) cases had WBC count (>5000/ µl). Whereas, the platelet counts were less than 50000/µl in 4 (3.9%) of cases, in 14 (13.6%) of cases had platelet counts less than 100,000/µl i. e. (50,000- 100,000/µl), and were between (100000- 150000/ul) in 12 cases.

Table (4): a study of the correlation between WBC and PLT in studied cases.

Age	WBC Count					LYMPH			PLT Count				Total
	<2000	2000-3000	3000-4000	4000-5000	>5000	<20%	(20-45)%	>45%	<50000	50000-100000	100000-150000	>150000	
	N (%)	N (%)	N (%)	N (%)	N (%)								
< 10	0 (0.0%)	2 (15.4%)	3 (23.1%)	4 (30.8%)	4 (30.8%)	4 (30.8%)	5 (38.5%)	4 (30.8%)	1 (7.7%)	1 (7.7%)	3 (23.1%)	8 (61.5%)	13 (12.6%)
10- 20	4 (11.8%)	8 (23.5%)	8 (23.5%)	5 (14.7%)	9 (26.5%)	16 (47.1%)	11 (32.4%)	7 (20.6%)	0 (0.0%)	3 (8.8%)	2 (5.9%)	29 (85.3%)	34 (33.0%)
21- 30	6(23.1%)	6 (23.1%)	2 (7.7%)	5 (19.2%)	7 (26.9%)	11 (42.3%)	8 (30.8%)	7 (26.9%)	0 (0.0%)	6 (23.1%)	1 (3.8%)	19 (73.1%)	26 (25.2%)
31- 40	4(25%)	2 (12.5%)	3 (18.8%)	2 (12.5%)	5 (31.3%)	6 (37.5%)	5 (31.3%)	5 (31.3%)	1 (6.3%)	3 (18.8%)	2 (12.5%)	10 (62.5%)	16 (15.5%)
41- 50	1(10%)	1 (10%)	5 (50%)	0 (0.0%)	3(30%)	3 (30.0%)	5 (50.0%)	2 (20.0%)	1 (10%)	1 (10%)	2 (20%)	6 (60%)	10 (9.7%)
> 50	1(25%)	1(25%)	1 (25.0%)	0 (0.0%)	1(25%)	1 (25.0%)	3 (75.0%)	0 (0.0%)	1 (25%)	0 (0.0%)	2(50%)	1(25%)	4 (3.9%)
Total	16 (15.5%)	20 (19.4%)	22 (21.4%)	16 (15.5%)	29 (28.2%)	41 (39.8%)	37 (35.9%)	25 (24.3%)	4 (3.9%)	14 (13.6%)	12 (11.7%)	73 (70.9%)	103 (100%)

As for biochemical parameters table (5), there was found an increase in the level of SGOT > 40 U/L in (42.72%) cases and SGPT > 40 U/L in (34%) cases among 103 patients with confirmed dengue infection.

In most studies, it was commonly confirmed that AST (SGOT) levels in dengue virus infection seemed to be higher than ALT (SGPT) levels, which was similar to our result [32, 33].

Other studies recorded the level of higher SGOT and SGPT liver enzymes separately for each one in (46.4% /51.1%) and (68% / 71%) in dengue confirmed patients respectively by [34, 35]. While other studies observed the level of liver enzymes elevation was lower

than described in the present study by Abdallah et al., [36] and Ferede et al., [37] whose seen higher levels than the normal values of AST / ALT in (9.9% / 14.8% and 45.1% / 17.6%) of the patients.

Wong et al., [13] suggested that dengue infection typically requires a moderate, self-limiting pathway in adults. Where transaminase elevation is common in transient patients, most dengue patients have been found to be mild to moderate, and in most patients, the volume of AST was higher than that of ALT when AST was released from the weakened monocytes. This can be used to separate dengue from acute hepatitis

caused by hepatoviridae A, B, and C, in which the AST / ALT ratio is reversed.

Increased liver enzymes have also been reported in several studies, so increased liver transaminases could be associated with secondary infection [7].

Also to evaluate the degree of kidney damage in dengue infection we attempted to measure serum creatinine and urea levels. Our data revealed that the majority of patients had normal serum creatinine levels about 68.9% of patients, but it was increased in 5.8% of patients. As for blood urea levels, the majority of patients had normal blood urea levels about 96.1% of patients, whereas, it was increased in 3(2.9 %) of patients table (5).

our results showed that only a very low number of cases showed a rise in serum creatinine and urea levels in 5.8% and 2.9% of cases, respectively. our results showed that only a very low number of cases showed a rise in serum creatinine and urea levels in 5.8% and 2.9% of cases, respectively. This is similar to another study that was observed in a limited number of cases that had an increase in serum creatinine and urea levels by [36].

In Thailand, a study performed by Futrakul et al., [38] recorded mild elevation in serum creatinine in 43% of 24 cases with DHF. Also, levels of serum creatinine and blood urea (BUN) increased was 19.6% and 14.7% respectively of cases in a study performed by [36]. As well as in 1.4% of patients showed a rapid rise in serum creatinine levels above baseline within 48 hours of hospitalization by [39].

Table (5): Various Biochemical parameters among studied dengue patients.

parameters	SGOT	SGPT	Urea	Creatinine
Range	Upto 40U/L	Upto 40U/L	10-50mg / dl	0.6-1.1mg/dl
Number cases	N (%)	N (%)	N (%)	N (%)
Normal	59 (57.28%)	68 (66.02%)	99 (96.12%)	71 (68.93%)
Increased	44(42.7%)	35(34%)	3(2.9%)	6(5.8%)

Table (6): A Comparison between mean of biochemical parameters with age groups of dengue patients.

Parameters		SGOT	SGPT	Urea	Creatinine
Normal Range		Upto 40U/L	Upto 40U/L	10-50mg \ dl	0.6-1.1mg/dl
Group	N (%)	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
≤ 10	13 (12.6)	↑42.85 ±20.62	36.92 ± 12.84	17.73 ± 6.27	0.51 ± 0.11
11 - 20	34 (33)	39.50 ± 21.39	31.00 ± 13.00	21.50 * ± 7.84	0.63 ± 0.17
21 - 30	26 (25.2)	↑45.38 ± 22.31	38.46 * ± 18.61	16.18 ± 6.23	0.75 * ± 0.20
31 - 40	16 (15.5)	↑56 * ± 33.72	↑41.19 * ± 18.20	22.25 * ± 9.98	0.81 * ± 0.20
41 - 50	10 (9.7)	↑41.50 ± 18.23	39.90 * ± 19.01	26.32 * ± 9.65	0.97 * ± 0.28
≥ 51+	4 (3.9)	↑76.50 * ± 14.84	↑57.75 * ± 5.85	32.70 * ± 21.13	1.10 * ± 0.23
Male	54 (52.4%)	52.5 4 ± 26.12	42.44 ± 17.03	21.59 ± 9.80	0.76 ± 0.25
Female	49 (47.6%)	37.9 6 ± 19.81	31.24 ± 13.93	19.72 ± 8.61	0.68 ± 0.22
Total	103 (100)	45.60 ± 24.34	37.12 ± 16.54	20.70 ± 9.26	0.72 ± 0.24

Values are presented as mean ± standard deviation. * = a significant difference from the total average for each parameter (P<0.05).

limitations:

one of the limitations of our study, it was limited to a single-center, therefore it wasn't including patients who visited outpatient clinics and other hospitals. Although this effort is one of the few efforts to study some of the hematological and biochemical profiles of dengue viral infection, it hadn't including clinical features, which should be done in the future for a better understanding of the presentation of dengue viral infection in this district.

Conclusion:

Dengue fever is a growing health problem in Yemen, it is spreading in many governorates.

The values of the peripheral blood cell parameters (thrombocytopenia and leucopenia) and aminotransferase (raised levels of SGOT and SGPT) are very helpful for dengue infection monitoring and can be useful in the prediction of prognosis, especially in limited-resource centers such as Yemen.

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دراسة بعض مؤشرات الدم لدى مرضى حمى الضنك في لحج / اليمن

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المُلخَص

أجريت هذه الدراسة لتقييم تأثير حمى الضنك على بعض المؤشرات الدموية والكيموحيوية على المرضى المصابين بفيروس حمى الضنك في مركز الجماهير الطبي / لحج خلال الفترة من يوليو إلى سبتمبر 2018.

تم فحص مائة وثلاثة حالة، والتي شملت 52.4% ذكور و47.6% إناث، تراوحت أعمارهم بين سنة إلى 60 سنة.

تضمنت الاختبارات التحليلية التعداد الكلي للدم (CBC)، ومستويات انزيمات ناقلة الأمين (GOT) و (GPT)، مستويات اليوريا في الدم، الكرياتينين.

أظهرت الاختبارات الدموية انخفاض عدد خلايا الدم البيضاء (WBC) الى أقل من 4000 / ميكرو لتر عند حوالي 56.3% من الحالات المرضية، تراوحت خلايا الدم البيضاء بين 2000-3000 / ميكرو لتر في حوالي 19.4%، أقل من 2000 / ميكرو لتر في 15.5% حالة، بينما في 21.4% حالة تراوحت خلايا الدم البيضاء 3000-4000 / ميكرو لتر.

كما ان عدد الصفائح الدموية (PLT) انخفض إلى أقل من 150000 / ميكرو لتر في 29.2% حالة، وتراوحت ما بين 50000 - 100000 / ميكرو لتر في 13.6% حالة، بينما في 3.9% حالة انخفضت الصفائح الدموية الى أقل من 50000 / ميكرو لتر.

أظهرت الاختبارات البيوكيميائية، زيادة في مستويات SGPT و SGPT عند 42.7% و 34% من الحالات المرضية على التوالي. في حين ارتفعت مستويات اليوريا والكرياتينين في الدم عند 2.91% و 5.83% من الحالات على التوالي.

نستخلص من ذلك، ان من العلامات التنبؤية لحمى الضنك تناقص عدد كرات الدم البيضاء والصفائح الدموية، وعلى العكس من ذلك رفعت مستويات ناقلات الأمين (SGOT) و (SGPT)، لهذا تعد مراقبة هذه المؤشرات مفيدة في تشخيص حمى الضنك من اجل تقديم رعاية صحية جيدة للمرضى.

الكلمات الرئيسية: حمى الضنك، مؤشرات الدم والكيمياء الحيوية.

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