



## The impact of gastrointestinal tract infection on acquiring dengue fever virus infection and haemorrhagic fever in Jeddah City, Saudi Arabia

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### ABSTRACT

This study aimed to investigate the relationship between gastrointestinal tract infection and dengue hemorrhagic fever. Dengue hemorrhagic fever is a syndrome caused by the dengue virus and primarily affects children below ten years of age and is spread by the *Aedes aegypti* mosquito. Gastrointestinal tract infection is a bacterial and parasitic infection that leads to gastrointestinal tract inflammation which involves the small intestine and the stomach. The relationship between the two can be manifested by gastrointestinal bleeding, acute pancreatitis, and fulminant liver failure. In this research work, 600 blood and feces samples of different ages and sex (7-8 worms) were collected from Jeddah city. From the blood samples, serum was made and stored at -20°C until use. The frozen sera samples were investigated for sero-detection of DENV-NS1 antigen as a rapid, sensitive, and cost-effective test to detect asymptomatic acute DENV-infected donors and anti-DENV IgM and IgG antibodies. Feces samples were processed for the detection of parasites. The data acquired from these samples of all the 600 participants were analyzed and interpreted, followed by statistical analysis using GraphPad Prism 5.0 software. All the values were considered significant, which showed a value of less than 0.05. Results were expressed as with the range. This article documents that gastrointestinal tract manifestations frequently occur among patients with dengue hemorrhagic fever. There are close relationships between gastrointestinal tract infection and dengue hemorrhagic fever. In current work, it was established that dengue fever leads to gastrointestinal tract bleeding in the presence of intestinal parasites. Therefore, failure to identify the patients with this infection early enough can lead to an increased morbidity and mortality rate.

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### Introduction

Dengue hemorrhagic fever (DHF) is a widespread arthropod-borne viral infection by the *Aedes aegypti* mosquito (1). This infection is caused by the dengue virus, which is perceived to belong to the Flaviviridae family. It manifests as a broad spectrum of diseases ranging from mild febrile infection and dengue fever to severe dengue, which involves capillary leakage and bleeding complications (2). Dengue fever is a seasonal pattern in which the peak infection ranges from July to November annually (3). Clinical manifestations of the DHF include severe fever and headache, skin rashes, myalgia, shock, and severe haemorrhage. Globally, WHO records over 25,000 deaths annually from DHF (4). In South Asian countries, DHF is considered the leading cause of hospitalization and death, especially among children, since it affects young people and children with low immunity levels (5,6). The DHF was first recorded in 1905 in Penang and has become one of the significant health concerns across the world due to increased infections (7). Perhaps; increased industrial and economic activities have led to a massive infrastructural development, which has created a conducive environment

for the *Aedes* mosquito breeding. In some cases, the dengue virus is asymptomatic, while in others, it is exhibited as an undifferentiated febrile illness (7-9).

For the last few decades, there has been an immense growth in population, increased urbanization rates, and inappropriate sanitary measures, which have led to increased cases of dengue infections. Due to the rise in disease burden, a typical manifestation of the gastrointestinal tract has been reported, characterized by related illnesses such as hepatitis, fulminant, acute pancreatitis and gastrointestinal tract infection (10). Research shows that gastrointestinal tract manifestations are commonly observed among patients suffering from DHF; there is a close relationship between DHF and gastrointestinal tract infections (11).

Gastrointestinal infection has been considered another threat to public health affecting the body's digestive systems. This bacterial and parasitic infection causes inflammation of the gastrointestinal tract for the small intestines and stomach, hindering effective digestion within the body. Previous studies revealed that there are over 200 million gastrointestinal tract infections in the U.S alone, with 3-6 million children dying worldwide due to gastrointestinal tract infections. This shows that gastrointestinal tract in-

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fection has emerged as one of the serious health concerns in the countries. Some of the symptoms of gastrointestinal infection include abdominal pains, vomiting, and diarrhea, with dehydration being the primary concern for gastrointestinal infections, which in turn requires rehydration to ensure water balance in the body (12).

Common worm infestations are considered a leading cause of anaemia due to blood loss in the infected population. The most prevalent parasite affecting the human population include whipworm like (*Trichuris trichiura*); schistosomiasis, which includes *S. japonicum*, *Schistosoma Manson* and *S. haematobium* and finally, the most prevalent of all the above are hookworm infections like *Ancylostoma duodenale* and *Necator americanus*. Clinically, worm infestations are considered one of the most significant causes of obscure acute gastrointestinal bleeding, especially in developing countries where the prevalence of intestinal worm infestation is comparatively high due to many factors, including socioeconomic factors as the main influencing and significant factor. Common intestinal worms, including roundworms (*Ascaris lumbricoides*), are the leading cause of chronic occult blood loss, which leads to anaemia (12). The second most prevalent intestinal infestation is hookworm (*Ancylostoma duodenale*) which leads to pancreatitis, intussusception, acute appendicitis, liver abscess, and biliary and gastrointestinal obstruction. These complications may lead to GIT bleeding and anemia (13,14).

In the intestine, hookworms attach to the intestinal mucosa, releasing an anticoagulant that helps them suck blood from the intestine, leading to intestinal bleeding. Roundworm, on the other hand, irritates intestinal mucosa as a result of the secretions from the worm leading to intestinal bleeding. Life-threatening lower GI bleeding is rare since it is usually intermittent and self-limiting (15). There have been increased dengue fever and dengue hemorrhagic fever, with typical manifestations resulting from the liver, kidney, and other digestive systems comprising the gastrointestinal tract (16). These manifestations have, in turn, led to increased morbidity and mortality rates across the world (9, 17). The gastrointestinal tract bleedings often occur, resulting from plasma leakage in case of severe dengue (10, 18). Dengue fever also affects the functioning of the stomach. The severity of DHF leads to the release of subserosal fluid, which collects and thickens the gall bladder. The prevalence of dengue fever in the stomach is exhibited on the first or second days when the patient experiences severe stomach pains with persistent vomiting (19). This also causes the growth of peptic ulcers on the stomach walls, preventing the release of digestive enzymes and inhibiting the proper functioning of the gastrointestinal tract (20). Therefore, this study aims to investigate the relationship between gastrointestinal tract infection and dengue hemorrhagic fever.

## Materials and Methods

### Ethical approval

To execute this study at the Faculty of Applied Medical Sciences, Umm Al-Qura University, Holy Makkah, Saudi Arabia, formal ethical approval was acquired from the Institutional Review Board (AMSEC 14-02-12-2013). Written and informed consent was obtained from all the participants before collecting samples. This study meets

the standards set by the Declaration of Helsinki for the participants and specimen collection.

### Clinical samples

The current research work included 600 participants from Jeddah city. Blood and stool samples were collected from each participant. Blood samples included approximately 10 mL of whole venous blood using sterile plain tubes without anticoagulant. All the acquired blood samples were allowed to clot for 30 minutes at room temperature. The clotted samples were later centrifuged at 3000 rpm for 15 minutes following the aseptic collection of serum which was transferred to sterile screw cap tubes of 5-mL capacity. All the processed blood samples were stored at  $-20^{\circ}\text{C}$  until further use. Ice boxes were used for the shipment of frozen samples to the Central Lab of the Faculty of Applied Medical Sciences, Umm Al-Qura University, Holy Makkah, Saudi Arabia, where different tests like sero-detection of DENV-NS1 antigen and asymptomatic acute DENV-infected donors<sup>24</sup> and anti-DENV IgM and IgG antibodies were performed (21).

### Serology testing to detect dengue

Antibodies against dengue virus were analysed with the help of commercially available DENV IgM capture enzyme-linked immunosorbent assay (ELISA), DENV Pan-E NS1 early ELISA and DENV IgG capture ELISA, respectively. All reagents were acquired from Panbio, Brisbane, QLD, Australia. According to the manufacturer's protocols, a fully automated ELISA (Human Diagnostics, Wiesbaden, Germany) was used in this research. Triplicate assays were used for the analysis of all samples (21).

### Detection of intestinal parasites

Stool samples were prepared by mixing 1 grams of the collected individual stool sample with approximately 8mL of 10% formalin. The prepared suspension was filtered using an FPC strainer, to which a 15 mL tube was attached to collect the filtrate. Once the stool sample suspension was filtered, approximately 3 mL of ether was added to the filtrate. The resultant mixture was then shaken vigorously for 1 minute following centrifugation for two minutes at 500 rpm. Parasites eggs and larvae were detected using thick, unstained wet mount of the sediment. A thin, iodine-stained wet mount of the sediment was used to detect For protozoan cysts using a microscope (22).

### Statistical analysis

The data were analyzed using Graph Pad Prism 5.0 software. All the values were considered significant which showed a value less than 0.05. Results were expressed as with the range.

## Results and discussion

The data acquired from all 600 participants were analyzed and interpreted. The results revealed that the study included participants with an age range 06 months to 96 years. This age range data was divided into 3 categories for statistical evaluation as shown in Table 1 which indicates the participants were in the age group between 16 and 55 (79.7%).

The gender data of the participants are shown in Table 2. Most of the study participants were male with 67.5%

**Table 1.** Data showing age groups of study participants.

		Age			
		Frequency	Percent	Valid percent	Cumulative percent
Valid	Child(9 -15)	60	10.0	10.0	10.0
	Adults (16-55)	478	79.7	79.7	89.7
	Geriatrics ( $\geq 55$ )	62	10.3	10.3	100.0
	Total	600	100.0	100.0	

**Table 2.** Data showing gender details of study participants.

		Gender			
		Frequency	Percent	Valid percent	Cumulative percent
Valid	Male	405	67.5	67.5	67.5
	Female	195	32.5	32.5	100.0
	Total	600	100.0	100.0	

**Table 3.** Data showing nationalities of study participants.

		Nationality			
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Saudi Arabia	431	71.8	71.8	75.5
	Egypt	60	10.0	10.0	85.5
	Yemen	22	3.7	3.7	89.2
	Pakistan	21	3.5	3.5	92.7
	Syria	4	.7	.7	93.4
	Bangladesh	12	2.0	2.0	95.4
	India	16	2.7	2.7	98.1
	Indonesia	6	1.0	1.0	99.1
	Turkey	4	.7	.7	99.8
	Philippines	1	.2	.2	100.0
	Jordan	5	.8	.8	
	Myanmar	2	.3	.3	
	Sudan	2	.3	.3	
	Palestine	3	.5	.5	
	Ethiopia	1	.2	.2	
	Malaysia	1	.2	.2	
	China	1	.2	.2	
	Sri Lanka	2	.3	.3	
	Tunisia	2	.3	.3	
	Nigeria	2	.3	.3	
Morocco	1	.2	.2		
Unknown	1	.2	.2	100.0	
Total		600	100.0	100.0	

**Table 4.** Data showing the percentage of the study participants with GIT symptoms.

		GIT Symptoms			
		Frequency	Percent	Valid percent	Cumulative percent
Valid	Yes	241	40.2	40.2	40.2
	No	359	59.8	59.8	100.0
	Total	600	100.0	100.0	

Table 3 represents the nationalities of the different participants. Most of the study participants belong to Saudi Arabia with a percentage of 71.8 followed by Egypt whose nationals contributed is 10% in this current study.

Table 4 represents the percentage of the study participants with GIT symptoms. The participants were exami-

ned for any kind of GIT symptoms like nausea, vomiting, abdominal pains, severe stomach pains accompanied by abdominal pain and GIT bleeding. The presence of any of the above symptoms was listed as "Yes" and absence was recorded as "No". The data indicated that 40.2% of the participants have one or more of the mentioned symptoms

**Table 5:** Data showing the percentage of the study participants with a complaint of dengue.

		Dengue virus symptoms			
		Frequency	Percent	Valid percent	Cumulative percent
Valid	No	401	66.8	66.8	66.8
	IgG	134	22.3	22.3	89.2
	IgM	65	10.8	10.8	100.0
	Total	600	100.0	100.0	

**Table 6:** Data showing the prevalence of parasites among the study participants.

		Parasites			
		Frequency	Percent	Valid percent	Cumulative percent
Valid	<i>A. lumbricoides</i>	74	12.3	12.3	12.3
	<i>S. mansoni</i>	51	8.5	8.5	77.5
	<i>T. trichiura</i>	65	10.8	10.8	88.3
	<i>T. saginata</i>	31	5.2	5.2	93.5
	<i>E. vermicularis</i>	39	6.5	6.5	100.0
	None found	340	56.7	56.7	69.0
	Total	600	100.0	100.0	

**Table 7:** Data representing the parameter estimates of the whole study.

		Parameter Estimates						95% Confidence Interval for Exp (B)	
Dengue <sup>a</sup>		B	Std. Error	Wald	df	Sig.	Exp (B)	Lower bound	Upper bound
No	Intercept	-1.936	0.683	8.036	1	0.005			
	Age	0.468	0.249	3.543	1	0.060	1.597	0.981	2.599
	Gender	0.179	0.233	0.594	1	0.441	1.196	0.758	1.887
	GIT symptoms	-1.275	.239	28.536	1	0.000	0.279	0.175	0.446
	Parasites	0.634	0.085	56.178	1	0.000	1.885	1.597	2.225
IgG	Intercept	0.488	0.903	0.292	1	0.589			
	Age	.374	0.319	1.378	1	0.240	1.454	0.778	2.716
	Gender	-.626	0.348	3.240	1	0.072	0.535	0.270	1.057
	GIT symptoms	-2.798	0.398	49.515	1	0.000	0.061	0.028	0.133
	Parasites	0.637	0.105	36.815	1	0.000	1.891	1.539	2.323

a. The reference category is: No.

of GIT disturbances.

Table 5 represents the percentage of the study participants with the symptoms and complaints of Dengue. Blood samples were collected and examined for the presence of dengue. The collected blood samples were analyzed at the Central Lab of the Faculty of Applied Medical Sciences, Umm Al-Qura University, Holy Makkah, Saudi Arabia, for sero-detection of DENV-NS1 antigen which is a rapid, sensitive, and cost-effective test to detect asymptomatic acute DENV-infected donors<sup>24</sup> and anti-DENV IgM and IgG antibodies. The data revealed that only 22.3% of the study participants had IgG positive and only 10.8% of the participants came out with IgM positive which means they actually had GIT symptoms at the time of sampling.

During the study, stool samples were also analyzed for the presence of any type of parasite. The data revealed that *A. lumbricoides* was more prevalent in the study participants with a prevalence percentage of 12.3 followed by *T. trichiura* which appeared in the stool samples of 10.8%. The parasite prevalence data in the stool samples are

presented in Table 6.

Table 7 summarizes the estimates of multinomial regression where dengue is the outcome variable and gender, parasites and GIT symptoms are repressors. We wish to check whether is there any statistically significant effect or correlation between GIT symptoms and parasites on Dengue. The outcome variable has three levels so we have run a multinomial logistic regression. GIT symptoms (P value=0.000) and Parasites (P value=0.000) both have a significant impact on Dengue as their P values are way too less than 0.05 showing the significance of the variables. While gender and age group have no significant impact on dengue. Gender and age in both of the cases where it is IgG or IgM are not significant while GIT symptoms and parasites are significant. Individuals with GIT symptoms are less likely to have dengue as the intercept is negative in both the cases IgG and IgM while people with parasites present are more likely to have dengue. The odds ratio of 0.279 for GIT symptoms indicates for every one-unit change in dengue, the odds of a person having GIT



symptoms decrease by a factor of 0.279. While the odds ratio of parasites indicates that one-unit change in Dengue increases the odds of parasites by a factor of 1.885.

Since this study investigates the prevalence and relationship between gastrointestinal tract complications and dengue hemorrhagic fever. The results have shown that gastrointestinal tract complications manifested in dengue fever. In our study, 58% of the patients that came up with IgM positive exhibited different gastrointestinal tract symptoms as exhibited in different studies conducted on the relevance of the relationship between DHF, GIT complications and worm infestations (23-27).

The results also revealed the specie that was most prevalent among the participants that were active dengue patients. The cross-tabulation of Dengue versus different parasites revealed that *T. trichiura* was the most prevalent parasite in the study participants (26.2%) that tested positive for IgM, followed by *S. mansoni* and *A.lumbricoides*, each with a prevalence percentage of 21.5 (24,25,27). Since previous studies have proved that the presence of parasites in the intestinal mucosa plays a significant role in the loss of blood from mucosa by inducing irritation through the production of different chemicals in the process of blood suction from the intestine. In dengue fever, the platelets are deficient in number, and it is hard to stop any hemorrhage, especially if some coagulant is involved. These findings explain the role of intestinal parasites in the DHF (23, 28, 29).

Dengue fever is considered self-limiting, and only a small number of patients pass through intensive care support. However, failure to identify the patients with infection early enough can increase morbidity and mortality rates. Consequently, the primary challenges to managing DHF are the burden of a low number of experts and clinicians conversant with this infection, a low number of hospital beds, and poor lab and transfusion support (23, 27-31).

### Limitation of the study

This study presents some limitations that should be considered before drawing any conclusions. Firstly, few studies have investigated a direct relationship between gastrointestinal tract complications and dengue hemorrhagic fever. Due to this, it is difficult to conclude that either the GIT complications are due to the presence of parasites or more factors trigger the worsening of the disease. A proper investigation into all the possible factors discussed in this paper can be used for medical and research purposes; hence, the conclusions drawn in this study should be used with many considerations. Secondly, the study does not conclude that social-economic factors affect the prevalence of DHF, such as age, environmental conditions, and gender. Hence, it is limited in the content covered as the main focus was to establish the connection between GIT complications and DHF, and the main highlight of the present research was the relation of GIT parasites to the prevalence of DHF. However, despite these limitations, the study determines several health concerns regarding the gastrointestinal tract linked with DHF. Therefore, this study can be helpful to policymakers, clinicians, and researchers who would like to address a rising concern regarding gastrointestinal tract infections and DHF.

This study concludes that gastrointestinal tract manifestations frequently occur among patients with dengue

hemorrhagic fever. One of the reasons for DHF could be the presence of intestinal parasites, as appeared in the current research, which could lead to gastrointestinal bleeding, among others. The study has illustrated one of the close relationships between gastrointestinal tract complications, intestinal parasites and DHF among patients with dengue infections. Gastrointestinal bleeding is a significant problem encountered among patients with DHF, resulting in increased mortality rates, and our study found that the presence of parasites in the intestine could be one of the different reasons for GIT bleeding. Therefore, it is necessary to consider this aspect while handling a DHF to reduce the disease's morbidity and mortality.

### Abbreviations

DHF: dengue hemorrhagic fever, WHO: World Health Organization

### Disclosure

The authors disclose that there is no initial conflict of interest for this study.

### Author contribution

The authors contributed equally to the drafting of the article and provided the final version to be published.

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### References

1. Dewi AP. The effectiveness of health education using audiovisual media on increasing family behavior in preventing dengue hemorrhagic fever (DHF). *Enfermeria Clinica*. 2019 Mar 1; 29:30-3.
2. World Health Organization. *Dengue hemorrhagic fever: diagnosis, treatment, prevention and control* 2nd ed. Geneva: WHO, 2017
3. Harapan H, Michie A, Mudatsir M, Sasmono RT, Imrie A. Epidemiology of dengue hemorrhagic fever in Indonesia: analysis of five decades data from the National Disease Surveillance. *BMC Res Notes*. 2019 Dec; 12(1):1-6.
4. Gibbons RV, Vaughn DW. Dengue: an escalating problem. *BMJ* 2002; 324: 1563-66
5. Weerasinghe WS, Medagama A. Dengue hemorrhagic fever presenting as encephalitis: a case report. *J Med Case Rep*. 2019 Dec; 13(1):1-6.
6. Weerasinghe WS, Medagama A. Dengue hemorrhagic fever presenting as encephalitis: a case report. *J Med Case Rep*. 2019 Dec; 13(1):1-6.
7. Ooi ET, Ganesanathan S, Anil R, Kwok FY, Sinniah M. Gastrointestinal manifestations of dengue infection in adults. *Med J Malaysia*. 2008 Dec 1; 63(5):401-5.
8. Souza LJ, Alves JG, Nogueira RM, Gicovate Neto C, Bastos DA, Siqueira EW, Souto Filho JT, Cezário TD, Soares CE, Carneiro RD. Aminotransferase changes and acute hepatitis in patients with dengue fever: analysis of 1,585 cases. *Braz J Infect Dis*. 2004; 8:156-63.
9. Naz S, Zahoor M, Umar MN, Alghamdi S, Sahibzada MU, UIBari W. Synthesis, characterization, and pharmacological evaluation of thiourea derivatives. *Open Chem*. 2020 Jan 1;18(1):764-77.
10. Ali K, Ma'rufi I. Study of factors caused dengue hemorrhagic fever case study: Pasuruan, Jawa Timur-Indonesia. *J Med Bioeng*.

- 2016 Apr; 5(2).
11. Khurram M, Qayyum W, Umar M, Jawad M, Mumtaz S, Khaar HT. Ultrasonographic pattern of plasma leak in dengue hemorrhagic fever. *J Pak Med Assoc.* 2016 Mar 1; 66(3):260-4.
  12. Singh J, Singh H, Sukhija G, Jagota R, Bala S. Retroperitoneal haematoma in a patient with dengue hemorrhagic fever: a rare case report. *J Clin Diagnostic Res: JCDR.* 2016 Nov; 10(11): OD01.
  13. Kumar P, Charaniya R, Ghosh A, Sahoo R. Intravenous immunoglobulin responsive persistent thrombocytopenia after dengue Haemorrhagic fever. *J Clin Diagnostic Res: JCDR.* 2016 Apr; 10(4): OD10.
  14. Al-Araimi H, Al-Jabri A, Mehmoud A, Al-Abri S. Dengue hemorrhagic fever presenting as acute abdomen. *Sultan Qaboos Univ Med J.* 2011 May; 11(2):265.
  15. Tsai CJ, Kuo CH, Chen PC, Changcheng CS. Upper gastrointestinal bleeding in dengue fever. *Am J Gastroenterol.* 1991 Jan 1; 86(1).
  16. Prashanth VN, Manasa G. Study of gastrointestinal manifestations in Dengue fever. *Int J Adv Med.* 2019 Sep; 6(5):1476.
  17. Gasperino J, Yunen J, Guh A, Tanaka KE, Kvetan V, Doyle H. Fulminant liver failure secondary to hemorrhagic dengue in an international traveller. *Liver Int.* 2007 Oct; 27(8):1148-51.
  18. Samarasekara K, Munasinghe J. Dengue shock syndrome complicated with acute liver failure and kidney injury, infective endocarditis, and deep vein thrombosis: a case report. *J Med Case Rep.* 2018 Dec; 12(1):1-4.
  19. Teerasartipan T, Chaiteerakij R, Komolmit P, Tangkijvanich P, Treeprasertsuk S. Acute liver failure and death predictors in patients with dengue-induced severe hepatitis. *World J Gastroenterol.* 2020 Sep 7; 26(33):4983.
  20. Dalugama C, Gawarammana IB. Lessons learnt from managing a case of dengue hemorrhagic fever complicated with acute liver failure and acute kidney injury: a case report. *J Med Case Rep.* 2018 Dec; 12(1):1-8.
  21. M Ashshi A, Alghamdi S, El-Shemi AG, Almdani S, Refaat B, Mohamed AM, Ghazi HO, Azhar EI, Al-Allaf FA. Seroprevalence of asymptomatic dengue virus infection and its antibodies among healthy/eligible saudi blood donors: findings from holy makkah city. *Virology.* 2017 Feb 22; 811:178122X17691261.
  22. Garcia LS, Procop GW. Diagnostic medical parasitology. *Manual of Commercial Methods in Clinical Microbiology: International Edition.* 2016 May 30:284-308.
  23. Chiu YC, Wu KL, Kuo CH, Hu TH, Chou YP, Chuah SK, Kuo CM, Kee KM, Changchien CS, Liu JW, Chiu KW. Endoscopic findings and management of dengue patients with upper gastrointestinal bleeding. *Am J Trop Med Hyg.* 2005 Aug 1; 73(2):441-4.
  24. Sari EF, Syam AF, Nainggolan L. Cause of upper gastrointestinal tract bleeding in dengue hemorrhagic fever patient. *Indones J Gastroenterol Hepatol Dig Endosc.* 2008 Jan 4; 9:30-4.
  25. Lim CH, Benjamin NH, Kan FK. Upper gastrointestinal haemorrhage in severe dengue: To scope or not to scope? *Med J Malaysia.* 2017 Feb 1; 72(1):55-7.
  26. Nawal CL, Meena PD, Chejara RS, Jain S, Marker S, Tuteja V. Dengue Fever as a Rare Cause of Acute Pancreatitis. *J Assoc Physicians India.* 2018 Oct 1; 66(10):82-3.
  27. Prashanth VN, Manasa G. Study of gastrointestinal manifestations in Dengue fever. *Int J Adv Med.* 2019 Sep; 6(5):1476.
  28. Nimir AR, Aziz MS, Tan GC, Shaker AR. Massive lower gastrointestinal bleeding attributable to heavy whipworm infection and Salmonella typhico-infection: a case report. *Cases J.* 2009 Dec; 2(1):1-4.
  29. Islam MT, Quispe C, Herrera-Bravo J, Sarkar C, Sharma R, Garg N, Fredes LI, Martorell M, Alshehri MM, Sharifi-Rad J, Daştan SD. Production, transmission, pathogenesis, and control of dengue virus: a literature-based undivided perspective. *BioMed Res Int.* 2021 Dec 15; 2021.
  30. Mohamed AM, Ahmed MA, Ahmed SA, Al-Semany SA, Alghamdi SS, Zagloul DA. Predominance and association risk of Blastocystis hominis subtype I in colorectal cancer: a case control study. *Infect Agents Cancer.* 2017 Dec; 12(1):1-8.
  31. Prasathkumar M, Raja K, Vasanth K, Khuroo A, Sadhasivam S, Sahibzada MU, Gawwad MR, Al Farraj DA, Elshikh MS. Phytochemical screening and in vitro antibacterial, antioxidant, anti-inflammatory, anti-diabetic, and wound healing attributes of Senna auriculata (L.) Roxb. leaves. *Arab J Chem.* 2021 Sep 1; 14(9):103345.