Role of Ultrasound in Common Fever Pathologies: Dengue, Malaria, Hepatitis and Typhoid Fever

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Abstract: Background and objective: The objective of the following study is to determine the use of ultrasound as an important adjunct to clinical and laboratory diagnosis of major causes of fever and in predicting the severity of the disease by correlating imaging features with laboratory findings. Methods: In our study 40 patients (Ten of each pathology) of age between 20 to 50 years, who presented with fever and serologically diagnosed were referred for ultrasound scanning of the abdomen and thorax, and the findings were analysed. Result: Typhoid-Ultrasonographic findings were hepatomegaly-splenomegaly, well distended gall bladder with thickened wall, oedematous wall thickening of terminal ileum, ileo-caecal junction and caecum, multiple rounded hypoechoic mesenteric lymph nodes and. Dengue - Ultrasonographic findings were gall bladder wall thickening, bilateral pleural effusion, peritoneal free fluid, Hepato-Splenomegaly and pericardial effusion. Malaria -Ultrasonographic findings were huge splenomegaly with hepatomegaly. Viral hepatitis A and E- Ultrasonographic findings were collapsed gall bladder with thickened wall, pericholecystiticoedema, periportal lymph nodes and hepatomegaly. Conclusion: Though serological tests will definitely diagnose the cause of fever, due to its unavailability in all parts of India especially in the small set-ups, Ultrasonography findings can provide the basic idea about the pathology and can help in starting the appropriate management as soon as possible. [D Revdiwla Natl J Integr Res Med, 2018; 9(1):45-51]

Key Words: Ultrasonography, fever, dengue, malaria, hepatitis, typhoid, serological tests.

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Introduction: The objective of the following study is to determine the use of ultrasound as an important adjunct to clinical and laboratory diagnosis of major causes of fever and in predicting the severity of the disease by correlating imaging features with laboratory findings. In my study I have taken four most common causes of fever in India. They are diagnosed by clinical presentation; however serological diagnosis forms the basis of confirmation. However, due to cost factors and limited infrastructure, serological tests are not available in most part of the country. Non-invasive imaging technique ofultrasonography (USG) is very important in diagnosing these conditions, which is widely available across the country in smaller set-ups.

Methods: In this study 40 patients (Ten of each pathology) with age ranging from 20 to 50 years who presented with fever and serologically diagnosed were referred for ultrasound scanning of the abdomen and thorax, and the findings were analyzed.

All ultrasound examinations were performed with Siemens Antares and Philips IU 22 machines, using 3.5-5 MHz probes. Abdominal scanning was done after 6 h of fasting to allow better distension of gall bladder (GB)as well as for better evaluation of bowel wall, and lymphadenopathies. Gall bladder wall thickening was measured by placing the callipers between the two layers of the anterior wall. Thoracic scanning was done in either sitting or supine posture. Both the pleural spaces were evaluated through an intercostal approach. Pericardial space was also evaluated for effusion subcostally. Spleen and splenic vessels were evaluated in left lateral position. The spleen was measured in two oblique scans as its maximum length, depth and width. In adults, the ''4–7–11'' rule of thumb was also applied: a spleen thicker than 4 cm, wider than 7 cm and longer than 11 cm is considered enlarged (Lorenz 1991)[1].Hepatomegaly was defined as liver size greater than 15 cm in long axis for adult age group. Terminal ileum and ileo-ceacal junction were evaluated in right lateral position.

Results: 1.Typhoid Fever: 10 patients who were clinically and serologically tested for typhoid fever were examined by ultrasonography during 1stweek and repeat examination was done at 15th day, after treatment. Ultrasonographic findings were hepatomegaly without any focal liver lesion (n=6), splenomegaly of 13 to 17 cm without any focal lesion (n=10), well distended gall bladder with thickened wall with thickness of 4 to 5 mm (acalculuscholecystitis in n=3), oedematous wall thickening of terminal ileum, ileo-caecal junction and caecum (n=9), multiple rounded hypoechoic mesenteric lymph nodes (n=9), peritoneal free fluid (n=2).

On 15th day, follow up study revealed reduction in the size of mesenteric lymphadenopathy,spleen and hepatic size reduced to their normal levels and complete resolution of bowel in 8 patients, however one patient show increase in thickness of bowel and perforation with surrounding fluid with dense echoes and gall bladder wall thickening with no evidence of fluid in peritoneal cavity.

Table 1: Incidence of different sonographic findings in typhoid fever

USG findings	Hepatomegaly without focal lesion	Splenomegaly without focal lesion	Acalculouscholecystitis	Bowel wall thickening	Mesenteric lymphadenopathy	Peritoneal fluid
No of patients	n=6(60%)	n=10(100%)	n=3(30%)	n=9(90%)	n=9(90%)	n=2(20%)
15th day	Negative	Negative	Negative	Negativein 8. Perforation (n=1)	Reduce in size	Negative

Graph 1: Pie chart for ultrasonography in Typhoid fever

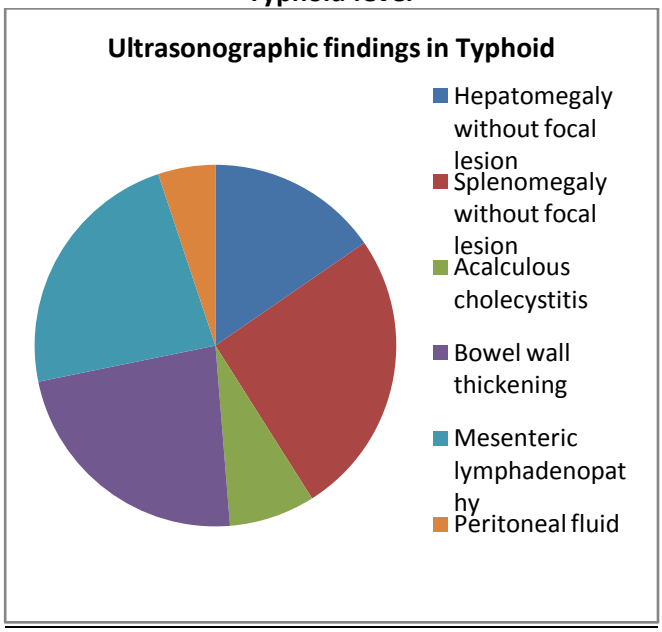


Image 1: Finding in case of typhoid Fever- oedematous bowel loops with intra peritoneal Free fluid

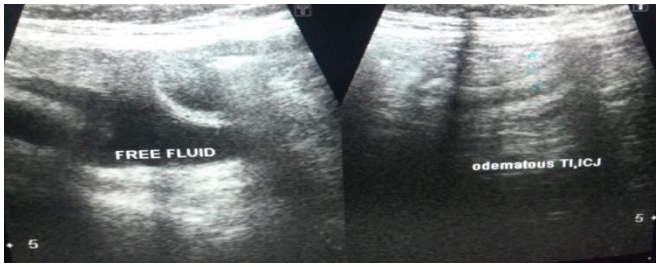
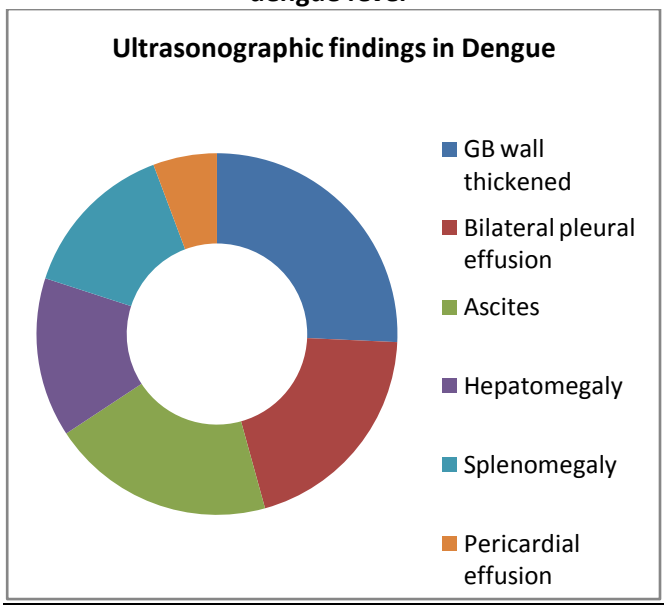


Table 2: Incidence of different sonographic findings in dengue fever

Total	Gall Bladder wall thickening	Bilateral pleural effusion	Ascites	Hepatomegaly	Splenomegaly	Pericardial effusion
n=10 100%	n=9 90%	n=7 70%	n=7 70%	n=5 50%	n=5 50%	n=2 20%

2. Dengue fever: Ten patients were clinically and serologically diagnosed as dengue fever came forultrasonography evaluation. Out of 10, ultrasonographic findings in 9 patient was GB wall thickening (90%), in 7 patients bilateral pleural Effusion (70%) and ascites (n=7, 70%), in 5 hepatomegaly (50%) and splenomegaly (50%) and in 2 patients there was pericardial effusion (n=2, 20%).

Graph 2: Doughnut chart for ultrasonography in dengue fever



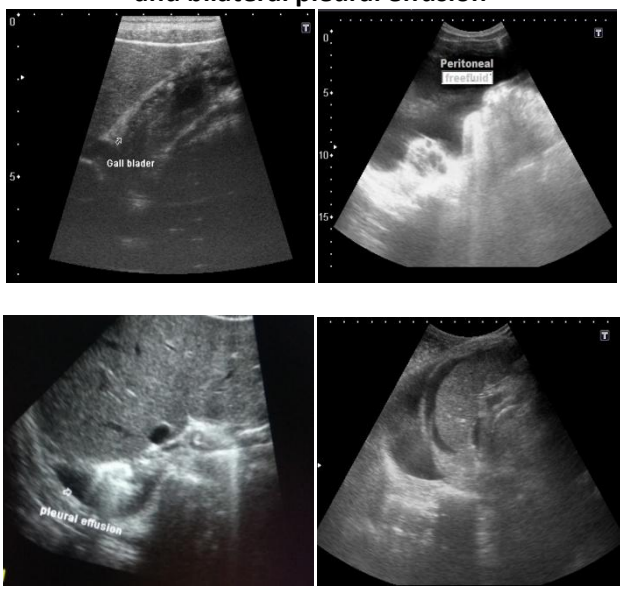
Features of dengue were correlated with platelets counts: Six patients whose platelet counts were below 60,000 were taken for USG evaluation, 5 of them show GB wall thickening (83.3%) and 4 of them show bilateral pleural effusion and ascites(66.67%). Three patient whose platelet counts were between 60,000 to 1,20,000 taken for USG evaluation, 3 of them show GB wall thickening(100%) and 2 of them show bilateral pleural effusion(66.67%).GB wall thickening and bilateral pleural effusion were common findings when platelet count were between 60,000 to 1,20,000.

Table 3: Correlation of Ultrasonographic findings with platelet counts

Ultrasonographic findings	<60,000	60,000-1,20,000	>1,20,000
Total	6	3	1
Gall bladder wall thickening	5	3	0
Bilateral pleural effusion	4	2	0
Ascites	4	1	0
Hepatomegaly	2	1	0
Splenomegaly	2	1	0
Pericardial effusion	1	0	0

In one patient with platelet count more than 1, 20,000, no sonological abnormality was detected.

Image 2: Findings in case of Dengue Fever: Gall bladder wall thickening, intra peritoneal free fluid and bilateral pleural effusion



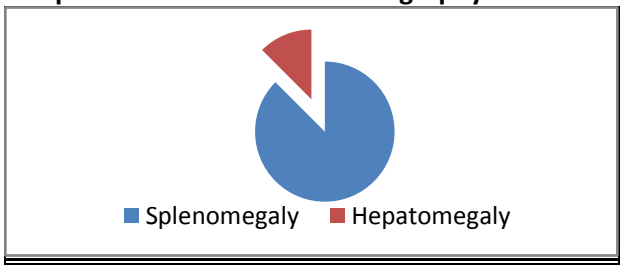
3. Malaria: Ten patients clinically and serologically diagnosed having malaria were taken for USG abdomen study.Out of 10, 7patients (70%) show huge splenomegaly with long axis diameter of 17 to 21cm.And 1 patient show hepatomegaly.

Serial ultrasound of 10 patients was done at day 21 after initiation of treatment, and the findings were compared to those during admission. Out of 10 patients, tested for splenomegaly 70% had huge splenomegaly. However on 21th day, percentage of splenomegaly drops from 70% to 30% and in one who suffered a falciparum malaria recrudescence splenomegaly persisted.

Table 4: Incidence of different sonographic findings in typhoid fever

Ultrasonographic Findings	Splenomegaly	Hepatomegaly
No of patients	7	1
%	70%	10%

Graph 3: Pie chart for Ultrasonography in malaria

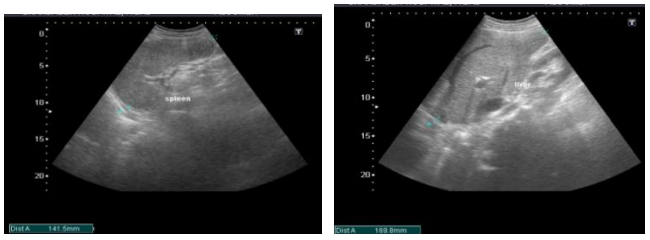


After 21 days follow up USG was performed.

Table 5: Follow up USG after 21 days

Ultrasonographic findings	Splenomegaly	Hepatomegaly
No of patients	3	4
%	30%	40%

Image 3: Findings in case of Malaria Fever- a)Splenomegaly b) Hepatomegaly without any focal lesion.



Graph 4: Pie chart for ultrasonography in viral hepatitis

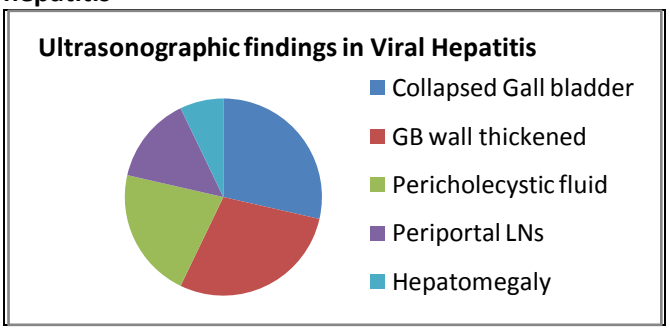


Image 4: Finding in case of Hepatitis-a) Collapsed Gall bladder with pericholecysticoedema and thickened wall .b) peripancreatic lymph nodes.

introduced by the oral route, multiplies in the intestinal lymphoid tissue, mainly in the ileo-caecal area and then disseminates systemically by either lymphatic or haematogenous route to localize in the liver, spleen or other organs.[2]The clinical features of Typhoid fever, while characteristic and suggestive of the diagnosis are, however, not pathognomonic. Inappropriate and inadequate administration of antibiotics, which is a common occurrence in our country, diminishes the possibility of culturing Salmonella from the blood and stool. This study demonstrates abdominal ultrasonographic changes associated with typhoid fever.

These changes are present early in disease. Our earliest examination was performed within the first few days of fever and all had positive findings. This study also shows that short period of adequate treatment may but not necessarily revert the abnormal sonographic findings almost normal. The examination is of particular value in those patients who received inadequate treatment, thereby greatly reducing the chance of obtaining positive blood culture. The serological test, Widal is the only diagnostic test widely available. Widal test is usually positive only in the second week and rising Widal titters are required to make a definitive diagnosis.

4. Viral hepatitis: Ten patients who were serologically positive for hepatitis A and E were included in our study. Out of 10 , in ultrasonography 8 patients show collapsed gall bladderwith thickened wall(80%), 6 show pericholecystic fluid(60%) ,4 patients show periportal lymph nodes(40%) and 2 patients show hepatomegaly (20%).

Discussion: Typhoid fever: Typhoid fever is caused by Salmonella typhi and paratyphi bacilli and is endemic in many parts of the world. Salmonella typhi,

Table 6: Comparison with other study

Ultrasonographic finding of Acalculuscholecystitis in typhoid fever	A study from Bangalore[3].	In our study
	24%	30%

Puylaert et al. reported ultrasound findings in three patients from the United States with typhoid fever, revealing enlarged mesenteric lymph nodes and mural thickening of the terminal ileum. These observations lead to the conclusion the findings in typhoid fever are similar to those of non-typhoidal Salmonella, Campylobacter jejuni, and Yersinia enterocoliticacases[4]. Following this study, Tarantino et al. evaluated the clinical application of the signs of bowel wall thickening and/or enlarged mesenteric lymph nodes to diagnose typhoid fever by assessing the sensitivity (68%) and specificity (81%) of these findings in febrile patients. In these patients, mural thickening (4 to 6 mm) was observed in 36.8% of patients with typhoid fever[5]In our study splenomegaly (100%), bowel wall thickening and lymphadenopathy

(90%) were most common findings associated with typhoid. Perforation of ileum is a critical complication occurs in 3rd week of typhoid. At the present time, the mortality rate while declining, it still remains very high ranging from 1 to 39% with significant morbidity in spite of curative advancement[6].Our study show lower incidence of intestinal perforation (1.2%) this could be due to that all patients were examined in their first week of illness where perforation is rare.Although the sonographic features are not specific for typhoid fever and the differential diagnosis include tuberculosis, Crohn's disease, lymphoma, and many of non-typhoidal salmonella but the clinical findings of these conditions usually do not mimic those of typhoid fever moreover in endemic areas combination of sonographic findings are typical enough to justify initiation of treatment and is fairly safe to say that normal ultrasound examination early in the course of febrile illness rules out typhoid fever.

Malaria: Malaria is a parasitic disease and is spread to human through the bite of an infected Anopheles mosquito. Bite of the mosquito releases plasmodium parasite in the blood stream. The parasites maturate in liver and further infect the RBCs and causes parasitemia. All these processes take 10 days to 4 weeks, so patients develop symptoms of high grade fever, chills, vomiting, sweating and diarrhoea 10 days to 4 weeks after the bite of the mosquito. General practitioners frequently have more rapid access to ultrasonography than to immediate performance of appropriate malaria diagnostics test by an expert microscopy of stained thick and thin blood films. Real-time ultrasonography provides immediate results, whereas drying and subsequent staining of blood films may take an hour and more, if at all available in the service.

Table 7 : Comparison with other study

Ultrasonographic findings	The studyconducted in Heinrich Heineuniversity, Germany[7]		In this study	
	On admission	On 21st day	On admission	On 21st day
Splenomegaly	82.76%	64.52%	70%	30%
Hepatomegaly	2.6%	8.66%	10%	40%

In above studies hepatomegaly was seen in 4 out of the 10 cases (40%) which were subsequently higher as compared to those recorded on the day of admission. This difference highlights the fact that enlargement of liver is not an indicator of acuteness and that during the resolving and recrudescence phase of malaria a higher level of hepatic enlargement can be noticed. Spleen has been a time tested marker of endemicity of malaria.

Table 5: Incidence of different sonographic findings in viral hepatitis

Ultrasonographic findings	Collapsed Gall bladder	Gall bladder wall thickened	Pericholecystic fluid	Periportal Lymph nodes	Hepatomegaly
Number of patients	8	8	6	4	2
%	80%	80%	60%	40%	20%

Unlike other tropical and parasitic diseases, such as echinococcosis or schistosomiasis, the malaria patients did not exhibit specific ultrasonographic features, the main feature of malaria being non-specific splenomegaly. Ultrasonographically detected splenomegaly is not a reliable diagnostic criterion for malaria either—although splenomegaly occurred frequently in the malaria patients, its absence does not allow one to rule out malaria. However persistence of Splenomegaly 21 days after therapy was associated with a higher risk of malaria recrudescence or relapse. In summary ultrasonography in malaria is useful in endemic areas where serological testes are not early available and to know the worsening of condition even after the treatment during follow up study.

Dengue: Dengue is a viral disease transmitted to humans through the infected Aedesmosquitoes, principally Aedesaegypti. DEN is a single-stranded RNA virus with four distinct serotypes (DEN-1 to -4). These serotypes of the DEN belong to the genus Flavivirus, family Flaviviridae. Among them, genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections.[8]Clinically dengue manifests with sudden onset of high fever with chills, muscle and joint pain, intense headache, retro-orbital pain, and backache.

Fever usually lasts for about 5 days, but rarely for more than 7 days.Recovery is usually complete by 7-10 days. A small proportion of persons who have previously been infected by one dengue serotype develop bleeding on infection with another dengue serotype. This is termed dengue haemorrhagic fever (DHF).The ultrasound findings in DF include gall bladder wall thickening, pericholecystic fluid, minimal ascites, pleural effusion, pericardial effusion and Hepato-splenomegaly.

Table 6: Comparison with other study

Ultrasonographic findings in Dengue fever	study conducted by Santhoshet al. (2014) 96 seropositive patients[9]	In this study10 seropositive patients
Oedematous Gall bladder wall thickening	66.7%	90%
Ascites	64.5%	70%
Pleural effusion	50%	70%

The serological tests for dengue including non-structural protein-1 (NS-1) Ag test and dengue immunoglobulin G/immunoglobulin M is the mainstay in the diagnosis of dengue fever however hem agglutination inhibition antibodies usually appear at detectable levels by day 5-6 of febrile illness. Imaging features of dengue fever such as gall bladder wall thickening, ascites, pleural effusion, hepatomegaly and splenomegaly are reasonably accurate in the diagnosis of dengue fever. This helps in starting appropriate management of the patient as soon as ultrasound is done, especially in centres where high end laboratory facilities may not be available for serological confirmation. While serological tests are watborne viral Hepatitis is more common than blood borne disease.

Gall bladder findings are common in all type of Hepatitis. Collapsed gall bladder with increased wall thickness and pericholecysticoedema were mostconsistent finding. Several hypotheses havebeen proposed to explain the mechanism ofgallbladder wall thickening in patients with acuteHepatitis. One confirmatory in the diagnosis of dengue fever, ultrasound can be of value in the assessment of severity. The degree of thrombocytopenia showed a significant direct relationship to abnormal ultrasound features in our study.

Hepatitis: Hepatitis is a viral infection of the liver and is classified into 5 types, Hepatitis A, B, C, D and E. A different virus is responsible for each type of virally transmitted hepatitis. Hepatitis A and E are acute, short-term disease, transmitted by feco-oral root. Hepatitis E is particularly dangerous in pregnant women. While Hepatitis B, C and D are most likely to become ongoing and chronic and mainly transmitted by infected blood and body fluid. In our country hypothesis is that gallbladder wallthickening, together with a decrease in gallbladdervolume, occurs when hepatocyte injury at the time ofonset of acute hepatitis causes a temporary decreasein bile production and excretion[10, 11]. A secondhypothesis is that gallbladder wall thickening is dueto a direct injury and inflammation of the mucosaland muscular layers of the gallbladder by Hepatitisvirus contained in bile juice[12].

Table 7: Comparison with other study

Ultrasonographic findings in viral Hepatitis	The study conducted in Rome[13]	study conducted by (liver unit)National Academy of Medical Sciences, Bir Hospital Kathmandu, Nepal[14]	In this study
Collapsed Gall bladder with thickened wall	81%	>50%	80%
Pericholecystic fluid			60%

Ultrasound alterations are usuallytime-limited and reversible; a normal pattern is in fact restored in more than 60% of the patients within 20 days from the first ultrasound examination. Conversely, the persistence of an abnormalsonographic pattern after 30days is associated with a clinically protracted course of viral hepatitis.[13]

Serological markers Serological markers of Anti HAV IgMand Anti HEV IgM (by ELISA) were used to confirm the diagnosis of hepatitis A and E respectively. Thus, ultrasonogrphic findings are present in most of the acuteviral hepatitis. Gall bladder findings of increased wallthickness and pericholecysticoedema are verycommon. It can be used as auxiliary findings in case of acute viral Hepatitis. When serological

diagnosticfacility is not available it can back up in the diagnosiswhen clinically acute Hepatitis is suspected as well as persistence of abnormal sonographic pattern on follow up study indicate worsening of condition.

Conclusion: Serological tests provide definitive diagnosis to identify the cause of fever. However, when serological diagnosticfacility is not available in all parts of India especially in the small set ups as well as when results are positive in late stage of disease or high chances of false negative result due to inadequate previous treatment, Ultrasonography findings can provide the basic idea about the pathology and can help in starting the appropriate management as soon as possible. As well as by follow up study we can detect severity and status of the disease either there is worsening or improvement in condition. Though ultrasound not provide accurate diagnosis and may be normal in the early stage of disease, due to its easy availability and no radiation hazards ultrasonography can be used to at least know the outcome of the disease, early identification of any complication and to rule out other causes of fever.

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