

Algorithmic Approach for Evaluation of a Patient with Ascites: Expert Opinion by Egyptian Club of Ascites (ECA)

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Background and aims: Ascites is defined as pathologic accumulation of fluid in the peritoneal cavity; cirrhosis is the most common cause of ascites. Multiplicity of possible etiologies may necessitate a wide scale of investigations for such cases. Designing an algorithmic approach for ascites cases is warranted especially in limited-resources countries. The purpose of this consensus is to develop an algorithmic diagnostic workup for diagnosing adult patients with ascites .

Material and Methods: The Egyptian Club of Ascites (ECA) is a special interest group, founded in 2016 by prof. Nadia Abdelaaty Abdelkader. It is an experienced multi-disciplinary team and different Egyptian universities were involved. ECA is seeking to offer better management options and better quality of life to ascites-patients of different etiologies all over Egypt and neighboring

countries. A literature search was performed to identify and revise studies on the diagnosis of ascites, working subgroups were selected and repeated workshops were conducted.

Results: An initial diagnostic algorithm was designed by the working subgroups, a one-day conference in April 2017 was held by the ECA during which the algorithm was revised and modified using the voting method. The algorithm was validated in different university hospital, to test validity. A one-day consensus conference was held by the ECA in April 2018 during which the algorithm was finalized and approved by the group .

Conclusion: A consensus on the diagnostic workup of adult patients with ascites was developed by the ECA hoping that it would enable for a judicious use of different investigations in this field .

INTRODUCTION

Ascites is defined as abnormal accumulation of fluid in the abdominal cavity [1]; Decompensated liver cirrhosis is the most common cause of ascites (around 80% of cases). Furthermore, ascites is the most common complication of cirrhosis as more than 50 % of patients with cirrhosis will develop ascites within 10 years after diagnosis [2]. The mechanism of ascites in cirrhosis is multifactorial due to severe sinusoidal portal hypertension and hepatic insufficiency, they lead to a circulatory dysfunction characterized by arterial splanchnic vasodilation, decreased effective blood volume, renal vasoconstriction with resulting sodium retention, and finally extracellular fluid retention [3].

The development of ascites is an independent predictor of severe impairment of QOL (emotional stress, disturbed social life, disturbed working) [4]. Moreover, cirrhotic ascites is associated with increased morbidities such as hyponatremia, hepatorenal syndrome (HRS) and spontaneous bacterial peritonitis (SBP) and is linked with negative impact on survival (5-year survival 30%) [5].

Causes of ascites

In more than 80 % of cases of ascites, the underlying etiology is liver cirrhosis. The next common cause is cancer (10%), followed by heart failure (3%); tuberculosis (2%), dialysis and pancreatic disease (1%) in addition to other rare causes [6]. Myxedema and SLE rarely present with ascites, usually mild, need no special investigation or special treatment, and in both the clinical features of the disease predominates. Nephrotic syndrome: essentially a disease of children and needs no special workup. causes of ascites are shown in table 1

Evaluation of adults with ascites

Evaluation of adult patients presenting with ascites should include the following items:

- Clinical evaluation
- Imaging studies
- Laboratory studies
- Abdominal paracentesis and ascetic fluid examination

Clinical evaluation is an important initial step in evaluating patients presenting with a

clinical picture suggestive of ascites. Skillful history taking & physical examination may help to reveal the possible underlying etiology of ascites. The onset of ascites is very important because the causes of rapidly developing ascites are quite different of those of a slowly developing one (TB, malignancy, HCC, hepatic venous outflow tract obstruction, BCS and SOS. Signs indicating liver diseases may include spider naevi, palmar erythema, and splenomegaly while the presence of peripheral edema, jugular venous congestion, third heart sound and pulmonary rales may indicate cardiac ascites. The presence of fever, lymphadenopathy should be noted for infections and malignancy. More than 1.5 (liter) ascites usually can be detected by abdominal examination [3].

Pelvi-abdominal Doppler ultrasound is the initial most cost-effective imaging modality in evaluating patients with ascites. It may provide information about the etiology of ascites, signs of portal hypertension (splenomegaly, portosystemic collaterals) and help in guidance of paracentesis. Complementary cross-sectional imaging (CT, MRI) may be needed in some cases [7].

Laboratory studies are usually nonspecific but base-line investigations should be conducted including blood picture to evaluate the presence of leukocytosis and thrombocytosis in cases of suspected systemic infection, while cytopenia may indicate hypersplenism and portal hypertension. Liver functions particularly serum albumin and prothrombin time evaluation is important in liver associated ascites. Urinary protein quantitation in addition to renal functions is important especially in cases of suspected nephrotic syndrome. Assessment of thyroid function is important in suspected myxedema ascites [8]. Serum amylase and lipase may be evaluated in cases of suspected pancreatitis and many other investigations may be ordered according to the suspected diagnosis.

Abdominal paracentesis with ascetic fluid examination (physical & laboratory based) should be done in every case of ascites parallel to imaging studies. Ascitic fluid analysis should be done for cell count, total protein, albumin and cultures in all patients as well as other tests in selected cases. A serum to ascites albumin gradient (SAAG) ≥ 1.1 g/dl has 97% accuracy for diagnosis of ascites due to portal hypertension whether due to cirrhosis, BCS, SOS or PV

thrombosis, <1.1= peritoneal disease which is TB or malignant infiltrations [9]. A neutrophil count (250/ μ l cut-off) should be obtained in each diagnostic tap, to diagnose SBP [10&11]. Ascitic fluid-based tests as well as additional tests are summarized in table 2.

Imaging studies

Abdominal ultrasound is the first line imaging to detect the presence of ascites and its quantity. Moreover, it may differentiate between some causes of ascites especially portal hypertensive and non-portal hypertensive etiologies. Abdominal CT may add value in detection of malignant ascites. While Doppler US may be helpful in detecting thrombosis and vascular liver diseases. But the abdominal US and CT may not be helpful in detecting peritoneal carcinomatosis.

Laparoscopy

Laparoscopy is considered a minimally invasive technique for examination of peritoneal cavity and allow biopsy from peritoneum, liver, and some intra-abdominal lymph nodes in most of cases of un-explained ascites [12].

METHODOLOGY

The Egyptian Club of Ascites (ECA) is an experienced multidisciplinary team, founded in 2016 by prof. Nadia Abdelaaty Abdelkader aiming to unifying the guidelines regarding diagnosis and management of ascites. This will be reflected on Excellency in management of patients with ascites and offering them the best medical care and better quality of life.

The ECA vision is divided into three integrated phases:

Phase 1: construction of imminent group of academics and clinicians concerned with the management of ascites. The multidisciplinary consensus group included participants with expertise in the areas of Hepato-gastroenterology and inviting experts from other specialties concerned with ascites. At this stage, the group is connecting continuously by different ways including meetings, phone calls, webinars, emails, etc. Problem solving and discussion of difficult cases of ascites of unknown cause all over Egypt are the aims at this stage. An algorithm fitting the national resources is developed for diagnosis of ascites, to be an aid for primary care providers and specialist dealing with ascites cases.

A literature search was performed to identify and revise studies on the diagnosis of ascites. Working subgroups were selected and repeated workshops were conducted. An initial diagnostic algorithm was designed by the working subgroups, one -day conference in April 2017 was held by the ECA to revise and modify this algorithm using the voting method. The algorithm was applied in different university hospitals, to test validity. Algorithm was progressively revised through separate voting/commenting iterations and finalized at the consensus meeting. A one-day consensus conference was held by the ECA in April 2018 and the algorithm was finalized and approved by the group. A statement was accepted if >75% of participants voted.

Phase 2: Building an electronic network involving all experts and physician all over the country and abroad and starting data registry of cases of ascites of different etiologies for purposes of research and clinical trials. The ECA is establishing the Egyptian Ascites Registry, as a national, prospectively recruited observational cohort study with clinical, biochemical, radiological information using the online platform RED Cap representing the basis for multiple collaborative projects.

Phase 3: International connections are in the plan collaborative clinical and research work with International Club of Ascites (ICA).

The Egyptian Club of Ascites (ECA) had designed an algorithmic diagnostic workup for the evaluation of adult patients presenting with ascites in ECA conference 2017. This suggested algorithmic approach was deeply investigated and discussed in ECA conference 2018. Lastly, ECA experts from all centers in Egypt met on 14th November 2019, to put a consensus for an algorithmic approach for the evaluation of patients with ascites "The Egyptian club of Ascites (ECA) opinion".

The Experts put the statements that representing different aspects of ascites diagnosis and voted for each point of this statements, A. accepted strongly, B. accepted with reservation (needs modification), C. Undecided, D. non-accepted, E. non-accepted strongly. A statement is considered accepted without modifications if 75% or more experts accept strongly for it. These statements were classified as follows:

- Section 1: Clinical evaluation for ascites (3 statements)
 - Section 2: Imaging studies (10 statements)
 - Section 3: Laboratory studies (2 statements)
 - Section 4: Abdominal paracentesis and ascetic fluid examination (4 statements)
 - Section 5: Imaging (US\CT) or laparoscopy guided biopsies (1 statement)
- Recommendation statements for ascites diagnosis in Egypt. (Table 3)
- According to these statements, the algorithm was designed(Figure 1) .

Table (1): Causes of ascites.

Portal Hypertension:

Liver cirrhosis

Alcoholic hepatitis

Hepatic congestion (Congestive cardiac failure, constrictive pericarditis, sinusoidal obstruction syndrome and Bud chiari syndrome)

Portal vein thrombosis

Non-cirrhotic portal hypertension

Malignancy

Hepatocellular carcinoma

Peritoneal carcinomatosis

Mesothelioma

Metastatic liver disease

Other intra-abdominal malignancy

Pseudomyxoma peritoneii

Infections

Tuberculous peritonitis

Spontaneous bacterial peritonitis

Secondary bacterial peritonitis

Chlamydia

Miscellaneous

Pancreatitis

Nephrotic syndrome

Lymphatic obstruction

Urinary leakage

Hypoalbuminemia

Protein losing enteropathy

Severe malnutrition

Ovarian diseases

Familial Mediterranean fever

Vasculitis

Hypothyroidism

Eosinophilic ascites

Granulomatous peritonitis

Table (2): Initial ascetic fluid-based tests as well as additional tests.

Initial tests (II-2;1) ⁵	Additional tests ⁶
- Cell count with differentiation	- Glucose conc (malignancy, bowel perf, inf.)
- Total protein concentration	- LDH (malignancy, bowel perf, malignancy)
- Albumin concentration (and SAAG)	- Gram stain
	- Amylase concentration (Panc, bowel perforation)
	- Cytological exam (?? CEA)
	- Triglycerides (chylous ascites)
	- Bilirubin concentration(bowel or biliary perforation)
	- TB work-up

Table (3): Recommendations for ascites diagnosis in Egypt.**Section 1: Clinical evaluation for ascites****Statement 1.1**

Clinical evaluation is an important initial step in evaluating patients presenting with a clinical picture suggestive of ascites.

Statement 1.2

Skillful history taking & physical examination may help to reveal the possible underlying etiology of ascites.

Statement 1.3

At a volume of more than 1.5 (liter) ascites usually can be detected by physical examination

Section 2: Imaging studies**Statement 2.1**

Pelvi-abdominal Doppler ultrasound with color Doppler is the initial most cost-effective imaging modality in evaluating patients with ascites

Statement 2.2

Complementary cross-sectional imaging (CT, MRI) may be needed in some cases.

Statement 2.3

Liver coarseness, the irregular border and attenuated hepatic veins of liver can be clearly seen in case of (cirrhotic) ascites.

Statement 2.4

Prominent hepatic veins ending into dilated IVC denoting hepatic venous congestion.

Statement 2.5

Attenuated or thrombosed hepatic veins with IVC web or thrombosis suggesting Budd Chiari syndrome. Portal veins thrombosis.

Statement 2.6

Bilateral swollen kidneys with prominent papillae suggesting acute renal insult or nephritic syndrome.

Statement 2.7

Heterogenous pancreas with peri pancreatic fluid collection or left pleural effusion suggesting pancreatic ascites.

Statement 2.8

Omental heterogeneity or masses suggesting omental malignancy, best seen in the left hypochondrial region, peritoneal masses (, adhesions or septations) suggesting deposits or TB.

Statement 2.9

Intra-abdominal or mesenteric lymphadenopathy suggesting metastasis, lymphoma, or TB.

Statement 2.10

Internal echoes or adhesions in the ascitic fluid suggesting local cause of ascites or spontaneous bacterial peritonitis in the presence of cirrhosis.

Section 3: Laboratory studies**Statement 3.1**

Lab studies are usually nonspecific but base-line investigations should be conducted including CBC, Liver & renal profiles, Serum & Urine electrolytes (and) as well as assessment of thyroid function.

Statement 3.2

Other specific laboratory investigations e.g. tumor markers may be ordered according to the suspected diagnosis.

Section 4: Abdominal paracentesis and ascetic fluid examination**Statement 4.1**

Abdominal paracentesis with ascetic fluid examination (physical & lab- based) should be done parallel to imaging studies

Statement 4.2

Initial tests for ascetic fluid as cell count, total protein and albumin should be done for all patients.

Statement 4.3

Additional tests as (Glucose, LDH, Gram stain, Amylase, Cytological exam, CEA, Triglycerides, Bilirubin, TB work-up) may be needed in some cases

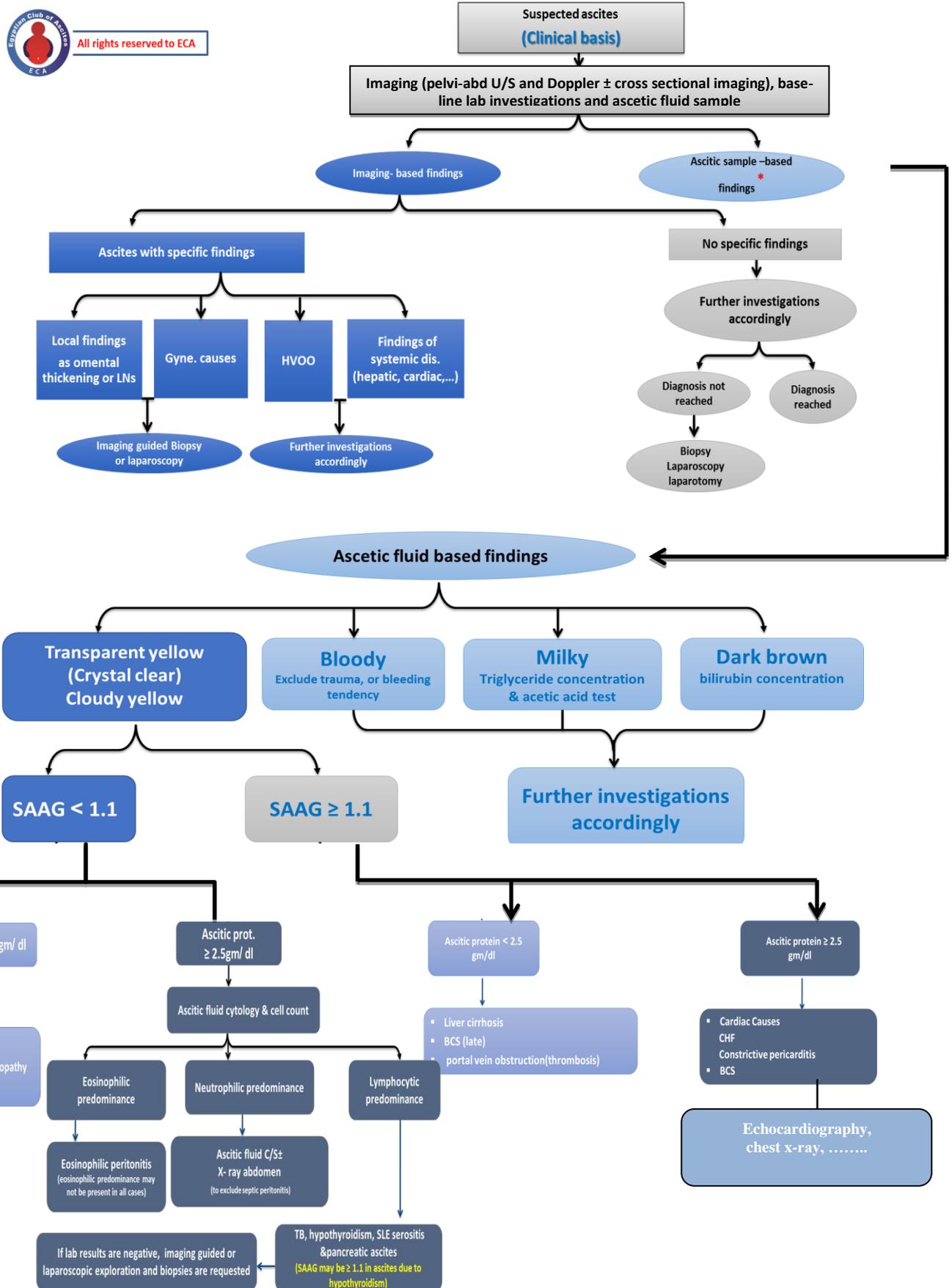
Statement 4.4

A serum to ascites albumin gradient (SAAG) ≥ 1.1 g/dl has 97% accuracy for diagnosis of ascites due to portal hypertension

Section 5: Imaging (US\CT) or laparoscopy guided biopsies**Statement 5.1**

Whenever, imaging and ascetic fluid-based tests fail to reveal the underlying etiology of ascites, either imaging or laparoscopy guided biopsies from any suspected intra-abdominal lesions is indicated.

Figure (1): The Egyptian Club of Ascites (ECA) algorithmic diagnostic workup for the evaluation of adult patients with ascites:



CONCLUSION

A consensus on the diagnostic workup of adult patients with ascites was developed by the ECA hoping that it would enable for a judicious use of investigational methods in this field. We just suggest an approach to diagnosis of ascites based on our expert opinions from different Egyptian universities according to availability, finance and effectiveness of different tools to reach the diagnosis in our centers. We have already used this algorithm in our university hospitals (Cairo, Ain Shams, Alazhar, Assuit, Minia , Zagazik, Benha,..) With great success. (ECA algorithm attached).

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Author's contribution:

Mohammad A. Sakr and Nadia Abdelaaty Abdelkader prepared and drafted the article, suggested the concept and designed the algorithm. Other contributing authors revised the article for important intellectual content.

Highlights

- The development of ascites is an independent predictor of severe impairment of QOL (emotional stress, disturbed social life, disturbed working)
- Evaluation of adult patients presenting with ascites should include the following items: clinical evaluation, imaging studies, laboratory studies, abdominal paracentesis and ascetic fluid examination.

- Laparoscopy is considered a minimally invasive technique for examination of peritoneal cavity and allow biopsy from peritoneum, liver, and some intraabdominal lymph nodes in most of cases of unexplained ascites
- The Egyptian Club of Ascites (ECA) had designed an algorithmic diagnostic workup for the evaluation of adult patients presenting with ascites in ECA conference 2017, deeply investigated and discussed in ECA conference 2018. Lastly, ECA experts from all centers in Egypt met on 14th November 2019, to put a consensus for an algorithmic approach for the evaluation of patients with ascites “The Egyptian club of Ascites (ECA) opinion”.

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