ORIGINAL ARTICLE

Global Gastroenterology

Liver diseases among Arab world, current state and unmet needs, a scoping review

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Introduction

A worrisome increase in liver diseases over the recent decades is noticed. Liver diseases are major causes of death and disability in Arab world, present with different patterns in all ages, both genders with variable socioeconomic status and culture.

Liver diseases have a significant burden of disease and costs worldwide, with variable etiologies and presentations, acute liver disease mainly due to viral hepatitis, while chronic liver disease due to alcohol and viral hepatitis. It's expected that drug induced liver injury (DILI) will be a major cause of acute hepatitis. Metabolic associated fatty liver disease (MAFLD) and alcoholic liver disease (ALD) will be the main causes of chronic liver disease in the world (1).

Deaths per year due to liver disease accounts for approximately 2 million deaths per year worldwide, half of them due to cirrhosis and it's complications and the second half is due to viral hepatitis and hepatocellular carcinoma (HCC) (2). However, increase in the global burden of both acute and chronic liver diseases is expected (2,3).

Viral hepatitides show a disastrous increase among the last decades, Acute hepatitis A showed a nearly 850% increase in incidence (3.8 in cases per 100,000 population in 2018) in comparison to 2014 (0.4 cases per 100,000 population), Acute hepatitis C showed a nearly 71% increase in incidence (1.2 in cases per 100,000 population in 2018) in comparison to 2014 (0.7 cases per 100,000 population), however acute hepatitis B showed a steady incidence rate in 2014 and 2018 due to vaccination (4,5).

Egypt is one of the top 6 countries in prevalence of chronic hepatitis C infection Viral hepatitis became 7th leading cause of death in 2013 in comparison to 1990 was 10th leading cause (6).

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MAFLD shows a terrifying increase in incidence reporting. MAFLD prevalence globally estimated 25.2%, with a prevalence above 30% in the Middle East (7,8). It's expected that MAFLD cases will increase from 83 million (2015) to 101 million (2030), with non-alcoholic steatohepatitis NASH cases increase from 1.5 million to 2.7 million (9).

Assessment of the global burden of compensated cirrhosis vs. decompensated cirrhosis is difficult. Liver cirrhosis related deaths are underestimated and hampered as many regions underestimate liver cirrhosis as the main cause of death (10). Compensated cirrhosis patients have a 5-fold mortality risk and decompensated cirrhosis have a 10-fold increased mortality risk than general population, irrelevant to comorbidity (11). Globally in 2017, 10·6 million cases with decompensated cirrhosis and 112 million with compensated cirrhosis, the highest age-standardized death rate among GBD was in Sub-Saharan Africa (12).

Liver cancer (primarily HCC) is the 6th leading cause of cancer worldwide in 2015. Men are affected more than women (5th leading cancer among men and 8th among women). It's the 4th most common cause of cancer deaths globally as it causes 810,000 deaths worldwide, also it's the 2nd leading malignant cause of absolute years of life lost, 2nd leading cause of cancer deaths among men and 6th among women worldwide (13). 5-year survival for liver cancer was only 18% (31% in localized tumors , 11% with regional spread and only 3% with distant metastasis), these data from The Surveillance, Epidemiology, and End Results (SEER) Program (14). Incidence and mortality due to liver cancer is expected to be doubled by 2035 globally and near **3** fold increase in middle east and Mediterranean region specifically (15). The Saudi Cancer Registry (2015) revealed that incidence of liver cancer ranked as the sixth most common cancer among Saudi males and 12th among Saudi women (16).

Liver diseases in Arab World represents a major health problem in morbidity and mortality. Liver cirrhosis is one of four main causes of death in Arabs, Egypt has the highest death rate due to cirrhosis among the world, 2/3rd of the admissions in Iraq are due to chronic liver diseases, by this order hepatitis B, alcohol, hepatitis C, immune hepatitis and metabolic diseases are major causes (17). Egypt has the highest incidence in chronic hepatitis C infection (18). In the Arab world, liver cancer caused a total of 17,638 deaths. 36% of them were due to HBV and 40% with HCV, Alcohol-associated cases was only less than 10% (19).

In Egypt, the total economic burden of HCV is $7.94 billion which is equivalent to 2.7% of Egypt GDP. Nearly $2.6 billion is the direct healthcare costs of HCV in Egypt which consume around 17.4% of the total health expenditure in Egypt (20). By 2025 a small reduction in HCV incidence is expected after 10 years, there will be 4.1 million chronic active HCV patients, 25% of them are cirrhotic, near 25 thousand have HCC, and a high annual number of deaths, about 25 thousand deaths. Unfortunately, the economic burden will be high, the direct costs will be estimated at $23.3 billion, while the total costs will be $48.3 billion between 2015-2025 (21).

In Egypt liver disease library, HCV-related and parasitic liver infestations literature represent the main interest of publications being the most important topics regard the prevalence and burden of the diseases. Publications of hepatocellular carcinoma (HCC) occupies the 3rd interest in Egyptian liver disease mapping. After that comes liver fibrosis/cirrhosis around (16%) of publications, less attention paid to other non-C, non-B viral infections, viral/parasitic co-infections, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH) and other liver diseases, although they have a major role influencing the outcome of liver disease, necessitating an urgent need for widening the scope of liver disease registry and study (22).

Regarding pediatric and hereditary liver diseases, In Oman, progressive familial intrahepatic cholestasis (PFIC) is the most common, followed by autosomal recessive polycystic disease of the kidney (ARPCDK) with congenital hepatic fibrosis (CHF), those represent (51%) of the presented hereditary liver diseases, followed by autoimmune liver disease, biliary atresia and metabolic liver diseases (23). This distribution is similar to Saudi distribution where PFIC is the most common one (35%) (24), also PFIC is reported in Arabs (25). Congenital hepatic fibrosis (CHF) with autosomal recessive polycystic disease of the kidney (ARPCDK) is the second one, reported in Kingdom of Saudi Arabia (26), and Kuwait (27).

Arab world literature about liver diseases is like a growing child. Viral hepatitides literature has the main interest due to its prevalence and burden in Arabs, liver cirrhosis and

cancers come then, but wide gaps are there in other liver disease categories. Literature about autoimmune liver disease (ALD) is deficient, continuous efforts needed to be performed for incidence, diagnostic procedures and clinical management beside geographic distribution (28). Liver cirrhosis mortality rate registry has a major uncertainty worldwide and in Africa specifically, therefore, there is a bad need to system registry to fulfill the gaps (29). Better surveillance of liver diseases in MENA can be achieved by improving the infrastructure of health care system including cancer registries and electronic recording of outpatient. Despite expensive treatment, it's easy and feasible to prevent liver diseases. Strengthening of the health care systems in the region can be performed for prevention and control (30). By studying publications in Arab world about liver diseases will reveal deficient parts and gaps in literature. We aim in this review to demonstrate the gaps in literature about liver diseases in Arabs for the future literature to fulfill the gaps for better registry and medical health.

Subjects and Methods

Methods

We searched PubMed, Scopus, Web of Sciences (WOS), EBSCO, and Wiley databases for relevant articles from 2011 to January 29th, 2021. We used different search terms that cover all liver diseases in addition to names of the Arab countries.

Study selection

All relevant studies that discuss any liver disease in any of the Arab countries were selected irrespective of age, sex, region, publishing year, or publishing language. We excluded review articles, non-human studies and publications study the surgically related liver diseases as liver transplantation and biliary diseases. Study selection was done by two groups from the search team in two steps: title and abstract then full text screening according to the inclusion criteria. Any disagreements were solved by discussion with the whole team.

Classification and Data extraction

After full text screening, all included studies were classified according to the main topic they discuss (acute liver failure, alcoholic liver diseases, viral hepatitis, non-viral hepatitis, non-infectious hepatitis, vascular liver diseases, and so on). Then relevant data was collected (authors, year of publishing, country, study type, and category of liver disease) by the research team.

Data analysis

As this is a scoping review, we aimed to collect the finding and provide an overview of the current state and unmet needs in liver disease research in the Arab countries rather than evaluating detailed or qualitative analysis. The collected data was summarized using data mapping showing the distribution of the studies by the liver disease category with subgroup data whenever possible.

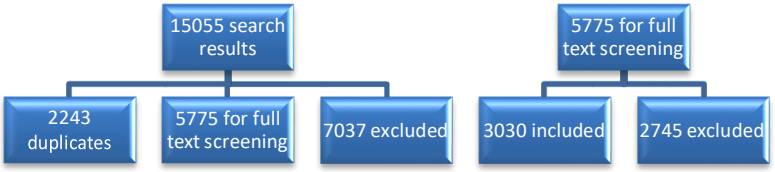

Chart 1: search strategy and review process

RESULTS

Research results found 15055 publications related to our work, in title and abstract screening step, 7037 publications were excluded, 2243 were duplicates. 5775 publications screened in the second step, full text screening, 3030 publications were included in our study, they were classified by topics according to the type of liver diseases, 1583 studies were about viral hepatitis (1284 studies were about hepatitis C virus, 279 studies were about hepatitis B virus and 20 studies were about the other viral). 94 publications studied the non-viral infectious liver diseases. Another 252 publications studied the metabolic liver diseases. The others were about acute liver failure, drug induced liver injury, liver cirrhosis and HCC.

1. Viral hepatitis

A- Hepatitis C virus infection (HCV)

Despite large number of excluded publications as they are abstract only, one thousand, two hundreds and eighty-four (1284) papers about chronic hepatitis C virus (HCV) infection are included in our review.

Included publications from 2011 up till now, stationary course of publications allover these years is noticed, in 2011 there are 89 publications, in 2012 there are 133 publications, in 2013 there are 117 publications, in 2014 there are 118 publications and so on, although, there is a noticed decline in publications in 2021, only 11 publications are included, may be due to decline in infection rate, good preventive measures, eradication of infection by the new direct acting antivirals and due to taking attention to COVID-19 pandemic.

Of the 1284 included publications, 999 papers (77.8%) nearly ¾ of included publications are from Egypt which has the highest rate of publication as Egypt is one of the highest rates of chronic hepatitis C infection among the Arab world. Kingdom

of Saudi Arabia (KSA) occupies the second place in publications about chronic hepatitis C infection, then comes Morocco, Iraq, Tunisia, Qatar, Lebanon, Libya, Kuwait, Jordan, Yemen, Sudan, Oman, Bahrain, Algeria, Palestine, United Arab of Emirates, Syria and Mauritania. Least publication is in Mauritania, only one paper, no publications is found from Djibouti, Somalia and Comoros.

Most of collected data about HCV infection in Arab world are observational studies (97.5%), only 32 papers are randomized controlled trials and clinical trials (2.5%). More than half studies are case control and cross-sectional studies, 368 (28.7%) of these studies are case control studies, 362 (28.2%) are cross sectional studies, 2.5% of publications are case reports and case series.

One fifth of included papers studying the epidemiology of HCV infection, either prevalence in general population, prevalence in specific groups of patients, Co-infections, risk factors of transmission of infection

HCV structure and diagnostic tests and techniques has the least attention in publication, only 8 papers (0.8%) of 1284 included papers are discussing the virus structure and diagnostic techniques (31–35).

In Arab World, HCV genotyping has less attention, studying the prognosis and prognostic factors, fibrosis detection and staging, available treatment and drug safety and efficacy and complications have a greater attention. Only 2.1% of publications asr studying the genotyping of HCV in arab world (36–41).

Available tratment options, efficacy ot treatment and safety have a high publication rate and importance, 241 papers (18.8%) are studying drug safety and efficacy among different populations, variable genotypes and different clinical situations. Regardin available tratment options, up to 2015, studies are about pegylated interferon and ribavirin efficacy (42–44) and side effects (45–47). From 2015 literature started to sstudy new directly acting antiviral agents efficacy (48–62). Recent research about DAAs is discussing a conflict of being a cause of HCC increase or not (63–66).

Prognosis, prognostic factors and complications of chronic HCV infection have the highest attention, they are being studied in more than half of publications, 433 (33.6%) papers are studying prognosis (67–70) and 238 (18.5%) papers are studying complications (71–74), however liver cirrhosis and hepatocellular carcinoma (HCC) are being studied in another part.

Detection of fibrosis and staging of it in chronic HCV patients is also important among arab world patients, 90 papers (7 %) are studying this topic (75–81).

B- Hepatitis B virus infection (HBV)

Global eradication of both hepatitis B virus (HBV) and hepatitis C virus (HCV) was aimed by the World Health Organization (WHO) by 2030. Several efforts worldwide are implemented to achieve these goals (82).

Reviewing the available literature regarding different HBV research areas in the Arab countries revealed 279 publications arising during the period from 2011 till 2021. The publication rate was almost stationary allover these years except in 2011 that could be attributed to the COVID-19 pandemic that drew the attention of all authors and publishers.

Of the 279 included papers, 95 papers (34.1%) are from Egypt (83,84) which has the highest rate of publication followed by KSA (85), Sudan (86), Tunisia (87), Iraq (88) and Morocco (89).

Most of collected studies about HBV infection in Arab world are observational studies cohort, case control or cross-sectional studies, only 2 papers are randomized controlled trials (90,91).

One third of included studies were focused about studying the epidemiology of HBV infection, either prevalence in general population (85–87), prevalence in specific groups of patients (age groups, specific locality, immunocompromised, transplant patients, hemodialysis (87) or cancer patients) risk factors of transmission of infection.

Viral genotyping and host genomics came second in frequency of publications (92,93). Furthermore, vaccination coverage, efficacy and awareness among healthcare workers, students and general population comprised about 15 % of publications (94,95). This could be justified by the life-long treatment of HBV and the importance of prevention of infection especially with the presence of effective vaccination program that was adopted worldwide and in the Arab countries as well (96).

There is paucity in the studies about different antivirals drugs used in HBV treatment despite its availability in most countries (97). This could be attributed to the long term follow up needed in HBV patients and most of the clinical studies performed were multicentric with international countries.

C- Hepatic viral infections other than HCV and HBV

About viral infections affecting the liver other than hepatitis C and hepatitis B , There were twenty original articles , about 50 % of them about hepatitis A virus (HAV) as it is more endemic in the Arab world , four of them were case reports, the other studies were from Egypt, Oman, Morocco, Lebanon, Iraq, Syria, Algeria and Tunisia (98–100).

One of them about epidemiology in Morocco (101), the rest are about treatment and emergent complications.

Other articles are about hepatitis E virus (HEV), cytomegalovirus, dengue fever, measles, herpes simplex virus, coronavirus, SEN virus and Bacillus Calmette Guerin . Most of them are case reports (102–105).

Definitely, there is a great gap in this point of research , especially covering epidemiology in different countries , genotyping , effect of treatment interventions , especially as regard endemic viruses (HAV, HDV and HEV).

2. Infectious liver disease other than viral hepatitis

Regarding infectious liver disease other than viral hepatitis, 94 studies were done in Arab world. Most of the studies were case reports (51.1%), followed by case control (13.8%), cross sectional (12.8%), prospective (8.5%),

retrospective (7.4%) and case series (5.3%). Only one study was randomized controlled trial (RCT) (106).
Regarding Countries, most studies were from Morocco (24.5%), Tunisia (19.1%), Egypt (18.1%) and KSA (12.8%) followed by Iraq (5.3%), Lebanon (4.3%), three publications for each of Yemen and United Arab of Emirates (UAE), 2 studies from Sudan, while other countries like Qatar, Jordan, Syria, Libya, Kuwait, Bahrain and Algeria (1 for each).

Most of the studies were related to hydatid cyst in the liver (61.7%) with its rupture at unusual sites as duodenum (107), peritoneum (108,109), cutaneous fistulation to the right Breast (110), abdominal wall and psoas muscle (111), inferior vena cava (112) or serious presentation as anaphylactic shock (113,114) and treatment modalities (115,116).

3. Acute liver failure (ALF) and acute on chronic liver failure (ACLF)

Fifteen studies in Arab world discussed acute liver failure. Out of them, 6 studies were case reports, 4 were cross sectional, 3 were prospective, one was case control, and one was retrospective.
Forty percent of studies were from Egypt (117–121), followed by two publications from each KSA, Iraq, Kuwait, Qatar and lastly one study from Yemen.

Three studies highlighted acute on chronic liver failure (ACLF) (118,121,122).
A publication in Qatar showed significantly reduced cortical thicknesses in multiple brain sites and significantly increased glutamate/glutamine (GLX) metabolites were observed in ACLF compared to those of controls at baseline study. Follow-up patients showed significant recovery in cortical thickness and GLX level compared to baseline study (122).
Another Egyptian publication demonstrated that HEV viraemia is a common cause of acute on chronic liver failure in Egypt. Hepatitis E virus RNA was detected in the sera of 13 of 100 presented with ACLF patients (13%) (118).

Another one analyzed 52 patients with ACLF and reported that infection was the main precipitating factors (38 cases; 73.1%) followed by variceal bleeding in 9 (17.3%). The 28-day mortality rates were 86.5% which was higher than what reported in the literature (121).

As regard ALF, an Egyptian study reported that Acute HEV infection was detected in 30 out of 300 acute hepatitis patients with unknown etiology (AHUE) (10%). Four out of 30 patients (13%) died due to fulminant hepatic failure within 3–6 weeks of hospitalization (123). A multicenter study in Kuwait showed the effect of N-Acetylcysteine (NAC) on mortality and liver transplantation rate in non-Acetaminophen induced acute liver failure. The NAC group included 85 patients and the control group included 70 patients. Recovery from ALF was reported in 82 (96.4%) patients in the NAC group with no need for liver transplantation. The success rate (transplant-free survival) in the NAC group was 96.4%. The success rate (transplant-free survival) in the control group was 23.3% as only 17 patients survived without liver transplantation. The remaining 53 (76.6%) patients did not recover from ALF, 37 (53.3%) of them had liver transplantation and 16 (23.3%) died (124).

A case control study in Iraq included 175 individuals (125 patients and 50 healthy control who represented the different stages of HBV infection (ALF, AHB, CHB and LC). IL-17A 197 A/G gene polymorphism G allele have a significant association in hepatitis B virus infection (125).

A first case report of fulminant hepatitis after laparoscopic Sleeve Gastrectomy associated with protein calorie malnutrition, multiple nutritional deficiencies in addition to concomitant use of therapeutic doses of acetaminophen (126).

Seven studies (46.7%) were done on pediatric patients (117,119,120,127–130). Four of them were case reports (117,127–129).

An Egyptian study included 126 children: 46 with acute HAV infection (13 out of them with fulminant presentation), 53 with AIH, and 27 healthy controls. Autoantibodies were detected in the majority of HAV (63.1%) and AIH (79.2%) groups. They conclude that Hypergammaglobulinemia and a high occurrence of autoantibodies are encountered in HAV infection. The higher gamma globulins in fulminant HAV, with an insignificant difference from that in AIH, suggest that a more aggressive immunological reaction is related to this presentation (119).

Another Saudi study did a retrospective study on early infantile liver failure (EILF) where 42 cases were identified. The etiology was indeterminate in 14 (33.3%) and established in 27 (64.3%): galactosemia (7 cases, 16.6%), tyrosinemia (5, 12%), neonatal hemochromatosis (NH) and hemophagocytic lymphohistiocytosis (HLH) [4 each, 9.5%], mitochondrial hepatopathy (3, 7%), and miscellaneous (5, 12%). LF resolved in 15 cases (35.7%), either spontaneously or in response to specific therapy, 23 (54.7%) died, and 4 underwent LT (9.5%). Galactosemia and tyrosinemia predicted good outcome (130).
Both pediatric chronic liver failure sequential organ failure assessment (pCLIF-SOFA) score (pCLIF-SOFA) and Pediatric End-Stage Liver Disease (PELD) scores at cut-off values > 8 and > 30 respectively on admission could predict death in children with acute liver failure (ALF) with high sensitivity. The pCLIF-SOFA score is better than the PELD score as a predictor of death in PALF and can be used for accurate selection of children with ALF who are in a real need of liver transplantation (LT) (120).
With respect to acute liver failure (ALF) and acute on chronic liver failure (ACLF) in Arab World, we should screen for underestimated viral infection as Hepatitis E and different types of treatable bacterial infections. We are in need for development of guidelines for proper management of acute liver failure and ACLF and urgent assessment for suitability for LT due to high mortality rates. We are in need for urgent application of validated scores that help in selection of candidates with ALF who are in a real need of LT. Randomized controlled trials (RCTs) are missing in Arab World.

4. Metabolic liver diseases

A- Metabolic associated liver disease (MAFLD)

The prevalence of MAFLD is increasing in an epidemic manner parallel to an increase in the prevalence of associated risk factors such as obesity, metabolic syndrome, and type 2 diabetes mellitus. About 20% to 30% of the patents, progress to develop nonalcoholic steatohepatitis (NASH). NASH can progress to fibrosis, cirrhosis, and even hepatocellular carcinoma. Some papers suggest that NASH may soon be the leading cause of cirrhosis, HCC (even without cirrhosis) and liver transplantation (LT) (131).

MAFLD is present in 20 to 40% of the general population in industrialized countries and is the most prevalent chronic liver disease (132). Among all subjects with MAFLD, features of non-alcoholic steatohepatitis (NASH) can be seen in 10-20%. The prevalence of NASH in Western countries is approximately 2-6% (133).

In our Arab world review, we included 228 papers. 145 papers (64%) of included publications are from Egypt. No available research discusses prevalence of MAFLD and NASH in Arab countries. Most of publications is about prevalence of obesity, metabolic syndrome and Diabetes mellitus. Most publications discuss demographics, risk factors and association of MAFLD with other health conditions (diabetes mellitus, obesity, viral hepatitis …. etc.,) (134,135)

Diagnosis:

Ultrasound of the liver has a high sensitivity and specificity (both approaching 90%) for detection of fatty infiltration but does not allow assessment for the presence or degree of inflammation and fibrosis (Davies 1991) (136).

Although, many publications available discuss the diagnosis of NAFLD using ultrasound, there is research gap in the assessment of biochemical markers and Non-invasive predictors of NASH. And no available evidence evaluates non-invasive markers such as HAIR index, BAAT index, BARD score, NFS calculated, APRI and The Enhanced Liver Fibrosis (ELF) score in the Arab world (137).

Mortality and morbidity in hospitalized patients with MAFLD are approximately 5 times higher than what is seen in the general population (138), Probably around 10% of MAFLD patients will progress to NASH over a period of 10 years. Cirrhosis later develops in 5-25% of patients with NASH and 30-50% of these patients die from liver-related causes over a 10-year period (138). Cirrhosis in patients with NASH can also decompensate into subacute liver failure, progress to hepatocellular cancer (HCC), and recur after liver transplantation. Steatosis alone is reported to have a more benign clinical course, with cirrhosis developing in only 1-3% of patients (138). Patients with NASH and fibrosis also have a significant risk for hepatocellular carcinoma (139).

Research gap is obvious in the pathogenesis of MAFLD, No clear data about the determinants of progression to steatohepatitis, liver fibrosis and hepatocellular carcinoma. Few research available on human genetic factors. No clear data about treatment of MAFLD. Only few publications available about Diet, physical exercise and lifestyle intervention recommendations to treat MAFLD (140).

Also, very few data available on pharmacological treatment of MAFLD (fenofibrate, fish oil, probiotics etc.,). Only two studies from Egypt study alterations of the intestinal microbiome and MAFLD. Few studies also observed the effect of laparoscopic sleeve gastrectomy (LSG) and bariatric surgeries on the resolution of MAFLD (141,142).

Important research gaps

- Health education and public health awareness are the essence to stop the increasing prevalence of NAFLD in Arab world. This represents a major research gap. No available publications discuss this important topic.
- NAFLD is found in 8–19% of non-obese people. The PNPLA3 gene polymorphism has a greater effect on liver fat in patients without metabolic syndrome. No available publication discusses non-obese NAFLD.
- Extrahepatic diseases associated with NAFLD/ NASH such as ischemic heart disease, obstructive sleep apnea and colorectal neoplasia. This association not well studied among Arab populations.
- There were no publications from Yemen, Comoros, Djibouti and Somalia.

B- Wilson's disease, hereditary hemochromatosis, Alpha1 antitrypsin deficiency and Cystic fibrosis

Only few publications, twenty-one publications discuss Wilson's disease, hereditary hemochromatosis, Alpha1 antitrypsin deficiency and cystic fibrosis in Arab world. Mostly case series and case reports. No available evidence discusses the pathophysiology, diagnosis, treatment, compilations and prognosis among Arab people (143–148).

C- Alcoholic liver disease (ALD)

Unfortunately, only three publications about alcoholic liver disease (ALD) are published among Arab countries, first one was a case report revealed a Moroccan alcoholic cirrhotic patient diagnosed when presented with acanthocytosis (149). Second one was in 2017 about a Lebanese alcoholic cirrhotic patient presented with torsade's de point during alcohol withdrawal (150). Last publication in 2020 in Iraq revealed that alcohol abuse cause impaired lipid profile which predispose to cardiovascular accidents, also it impairs liver enzymes causing liver dysfunction (151).

The very low reported number of publications about ALD is attributed to religious causes. Even the alcoholics can't confess their habit not only religiously but also culturally.

Lots of gaps about ALD among Arab world from diagnosis to pathophysiology, classifications, biomarkers, treatment lines, efficacy, prognosis and complications. Many

research points need to be investigated among Arabs.

5. Autoimmune liver diseases

Thirty eight publications among Arab world about autoimmune liver diseases, 26 publications about autoimmune hepatitis (AIH), 5 publications for each primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC), one publication about lupus hepatitis (152) which was case series and another about overlap syndrome (153) which was a case report also. Most of publications were from Egypt, Tunisia and KSA. Near half of publications were only in 2011 and 2013. 18 of 38 publications are case reports, the rest were prospective, retrospective, cross-sectional and observational. No randomized controlled trials were reported about autoimmune liver disease among Arab world.

Twenty six publications were about AIH, about one third of them were case reports (154–161). The second one third of publications were reported about the pediatric AIH (162–168). The last one third discuss the characteristics of the disease (169,170), poor prognostic factors and risk factors (171,172), biomarkers for diagnosis (173–175) and lastly complications of AIH (156). No reported publication about the experience of transplantation in AIH hepatitis and long term follow up.

As regard primary biliary cholangitis (PBC), only 5 publications among Arab countries, two publications were from Tunisia, two from Morocco and last one from Qatar. 4 of them were case reports (176–179), the last one was retrospective study detecting prevalence of antiphospholipid antibody level among PBC patients. Unfortunately, no randomized controlled trials, no prospective or observational studies, no studies reported about the diagnosis, biomarkers, disease characteristics, treatment efficacy and safety, complications of the disease and long term follow up. Lots of gaps in PBC publications among Arabs needs to be studied.

Another 5 publications were reported about primary sclerosing cholangitis (PSC) from different Arabian countries (180–184), two of them were case reports and the others were case control and cohort studies. They discussed the characteristics and evaluation of PSC with imaging modalities. No reported publications about complications, transplantation and long term follow up.

6. Toxic and drug induced liver injury

Fifty-three publications were reported about drug induced liver injury (DILI) and toxic liver diseases among Arabs. Around one third of them were from Egypt, then Tunisia, Qatar and Kingdom of Saudi Arabia. From 2011 to 2020, publications per year were nearly stationary but no reported publications in 2021. Near half of publications were case reports (185–189), but the others were variety of randomized controlled trials (190,191), prospective (192,193), retrospective (194,195), cohort (196–198) and observational studies studying the presentation, causes, diagnosis and outcomes of DILI but no studies in liver transplantation in DILI and toxic liver patients.

7. Vascular liver diseases

As regard research work about vascular liver disorders in Arab world, we have sixty-four original articles, twenty-eight of them are about Budd Chiari syndrome. Two publications were about hepatic artery diseases, one about ischemic hepatitis, one about congestive hepatopathy (199), and the rest about portal vein thrombosis and portal hypertension (200–203).

One of the papers about hepatic artery diseases is a case report from Tunisia (204), the other is a retrospective study from Egypt about management of hepatic artery thrombosis post transplantation (204).

The two studies were about congestive hepatopathy and ischemic hepatitis are case reports, one from Qatar and another from Egypt (199,204).

Budd Chiari studies are twenty-eight, most of them are from Egypt, especially due to presence of scientific group for Budd Chiari syndrome in Ain Shams University in Cairo. Four of them are case reports, the rest are cross sectional studies. two of them are discussing epidemiology, two about therapeutic interventions, four about diagnostic modalities, two about complications and the rest about associations and risk factors (205–209).

The rest of the studies are about portal vein hypertension and portal vein thrombosis, it may be due to the fact of endemicity of hepatitis C and B, with their complications of portal hypertension and thrombosis especially that associated with malignancy.

Most of studies about portal vein are from Egypt followed by Morocco and Tunisia, the upper hand is for cross sectional studies followed by cohort and case control studies.

Most of them are discussing portal hypertension and its complications, followed by portal vein thrombosis as regard diagnostic tools and therapeutic interventions.

We need more studies about role of anticoagulation in vascular disorders in hepatic patients, development of new markers for early prediction and diagnosis of thrombosis, to assess role of liver transplantation.

Also, we need more about congestive hepatopathy, ischemic hepatitis and their management with cardiology team.

8. Pediatric liver disease

Most of publications from Egypt, have discussed diagnosis and treatment outcomes. No Available data on prevalence, pathophysiology, genetic polymorphism and prognosis of pediatric disease among Arabs. Publications were mentioned each in its category, either metabolic, genetic, acute liver cell failure or chronic liver disease with its complications. The absence of data from population-based studies in Arab world highlights the need for further studies to reliably define the health service needs for this region and plan a cost-effective health care program (210).

9. Granulomatous liver diseases

It is considered one of the scarcest subjects as regards Arab publications with only four case reports published. Two from Tunisia, one from Bahrain and the last from Lebanon. Publication years were 2011 (211), 2018 (212), 2020 (213) and 2021 (214) with the rate of one per mentioned year. Two of them mentioned hepatic tuberculosis, either in isolated form

resembling hydatid cyst (213) or in concomitance with hepatocellular carcinoma (214), one about Langerhans' cell histiocytosis (211) and the last one about Bacillus Calmette-Guerin (BCG) infection after BCG bladder instillation (212).

There was no published data about sarcoidosis which is considered among the commonest causes of hepatic granulomas (215), nevertheless, some entities like primary biliary cholangiopathy and some of drug-induced liver injuries should be classified under the title of granulomatous liver diseases.

Many other less common etiologies were also mentioned in the literature without any Arab publications like talc, barium, and silicone from therapeutic and diagnostic procedures have also been found to be associated with this condition. Other causes include chronic hepatitis B and C infection, brucellosis, leprosy, histoplasmosis, coccidioidomycosis, schistosomiasis, amebic liver abscess, lymphoma, and malignant granuloma or even idiopathic (216).

We think that Arab authors should be encouraged to publish more and more of their case reports, collaborate to collect series of common etiologies and develop a common pool of database that would help to retrieve retrospectively enough information to facilitate further and more advanced forms of research and publications.

10. Liver diseases and pregnancy

Liver disease in pregnancy presents a real challenge for hepatologists. In review of literature in the Arab World, we found forty-seven original articles discussing different liver diseases that occurs during pregnancy, most of them (60%) investigating viral hepatitis among pregnant women either HBV (217–222), HCV (223–228) or HEV (229–231).

Nearly 25% of these papers were just reported cases of unique liver diseases in pregnancy like Fatty liver of pregnancy which was the most reported case in different countries; Tunisia (232), Oman (233), KSA (234), Jordan (235), Lebanon (236) and Morocco (237,238). Tunisia published a retrospective study in this life threating condition over 10 year period (239). Intrahepatic cholestasis of pregnancy was discussed in two papers from Egypt; one prospective study (240), another case control (241) and reported in one case from Lebanon (242).

Other unique liver diseases in pregnancy like pre-eclampsia and its associated complications and Hemolysis, Elevated Liver Enzymes, and Low Platelets Syndrome (HELLP syndrome) were also discussed in case series from Morocco, cross sectional study from Sudan (221,243) and finally case control from Egypt (244).

Vascular liver disease in pregnancy like Budd chiari syndrome was discussed and reported in two papers from Egypt (208,245).

Liver cirrhosis is not a contraindication for pregnancy, although cirrhotic women difficult to get pregnancy, only one prospective Egyptian study discussed maternal and fetal outcome in pregnant women with liver cirrhosis (246), and one reported case from Saudi Arabia of acute on top of chronic liver failure complicated by invasive fungal infection (247).

A lot of important topics of pregnancy associated liver diseases needs to be investigated in the Arab world, like Hyperemesis graviderum, pregnancy among cirrhotic patients, and post liver transplant with evaluation of both mother and fetal outcome.

11. Liver cirrhosis and its complications

Two hundred and eighty-one publications were included regarding liver cirrhosis and its complications among Arab world from 2011 to 2021. Most of publications were from Egypt (230, 82,9%), followed by 20 publications from KSA (7,1%). No publications from Jordan, Djibouti, Syria, Somalia, Comoros, Lebanon, Libya, Palestine, Kuwait and Mauritania. Egypt has the highest rate of publication due to increased prevalence of viral hepatitis and posthepatitic cirrhosis. From 2011 to 2021, publication rate was nearly stationary, but least publication was recorded in 2021 (7) and 2019 (9), mostly due to eradication of HCV after the era of direct acting antiviral drugs (DAAs). Most of studies were case control (29,2%) and cross sectional (22,8%) studies, the others were variable between cohort, prospective, retrospective and observational studies. There were (21, 7,5%) RCTs.

Sixty five publications studied the vascular complications of liver cirrhosis, for portal hypertension early detection either by invasive or non-invasive procedures and predictors of bleeding (248–250), invasive management with trans jugular intrahepatic Porto-systemic shunt (251,252) and rectal ozone(253), management of portal hypertensive gastropathy (254), gastric varices diagnosis and different modalities of management and survival (255–259), esophageal varices from early noninvasive prediction and diagnosis (260–267), management (268–273) and risk of rebleeding (274,275), small bowel varices (276), and portal hypertensive colopathy (277). Prediction of risk of portal vein thrombosis (278), diagnosis (201,279,280) and survival (281). Two publications studied portal hypertension and portal vein thrombosis in children (282,283). Another publication studied portal and splanchnic hemodynamics after partial splenic embolization in hypersplenism cirrhotic patients (284). Systemic vascular resistance and affection of carotid intima thickness were studied among Arabs (285,286), also pulmonary hypertension in cirrhotic patients (287).

As regard central nervous system affection, there were seventeen publications, most of them studied hepatic encephalopathy from early detection, diagnosis, management and prognosis (288–293), one article studied minimal hepatic encephalopathy in children (294). Also, sudomotor changes, extrapyramidal manifestations and depression were studied (295–297).

High-rate incidence of infections is recorded in cirrhotic patients. Most common infection recorded is spontaneous bacterial peritonitis (SBP) which is studied in detail from early detection, diagnosis, management and outcomes (298–303). SBP was studied among infants and children (304). Also, septic shock and fungal infection were recorded among cirrhotic Arabs

(247,305–307). The high rate of infections among cirrhotic patients is due to immune dysfunction occurs (308,309).

Renal affection of cirrhotic patients is common, hepatorenal syndrome (HRS) is the most studied one (310–313), HRS in children is a rare presentation (314,315). Also, acute kidney injury in cirrhotic patients is a challenging presentation (316–319).

Coagulopathy in cirrhotic patents is a major problem that we face from either coagulation defect or thrombocytopenia and platelet dysfunction (320–323). Facing pediatric cirrhotic patients with coagulopathy is a difficult situation (324).

Liver cirrhosis can cause multisystem affection, cardiopulmonary complications can occur secondary to liver cirrhosis, many publications among Arabs had studied the cardiopulmonary complications, as regard cardiac muscle affection and myocardial perfusion abnormalities (325–328), hepatic hydrothorax (329,330), affection of respiratory function (331–333) and hepatopulmonary syndrome (334)

While investigating the publications studying liver cirrhosis and its complications among Arabs, sporadic studies about metabolic bone mineral affection (335–337), fasting in Ramadan and liver cirrhosis (338,339), nutrition and malnutrition among cirrhotic patients (340,341), sleep pattern and disturbance (342,343), refractory ascites (344,345), stem cell transplantation and liver cirrhosis (346–348) and liver cirrhosis and fertility (349). Many studies about hepatocellular detection in cirrhotic patients which will be discussed later.

Liver cirrhosis and its complications is well covered among Arab world, we think that there are no gaps need to be fulfilled.

12. Hepatocellular carcinoma

In this review, 599 original articles and case reports related to HCC were included and published from 2011 to 2021. The publication rate was stationary from 2011 to 2016 and increased from 2017, while the maximum rate of publications is observed in 2020 which had 107 publications, however significant decline was observed during 2021. This decline in publication may be attributed to era of HCV treatment and paying attention to COVID-19 pandemic.

Of 599 reviewed HCC publications, 514 publications were from Egypt (85.80%). KSA was represented as the 2nd Arabian country for HCC publications with 28 publications (4.087%). Tunisia was represented as the 3rd Arab country with 14 HCC publications (2.59%), followed by Morocco (2.11%). There were 6 publications from Lebanon, 5 publications from Qatar, 3 publications from UAE, Algeria and Sudan each, 2 publications were from each Oman and Iraq. Finally, single publication was from each of Jordan, Yemen, Bahrain, Kuwait and Syria. Single shared multi-center study from Morocco, Tunisia and Algeria. There was no publication from Libya, Palestine, Mauritania, Djibouti, Somalia or Comoros.

In Arab word, 39.73% of study design was case control (238 studies), 27.37% was cohort (164 studies), 17.52% was cross sectional (105 studies), 8.01% was case reports (48 publications),1.83% was randomized controlled trials (11 studies), 1.83% was observational (11 studies), 1.16% was case series (7 publications), 1.13% was retrospective descriptive (7 studies) ,0.66% was comparative analysis (4 publications) ,0.33% was clinical trial (2 studies), 0.33% was pilot (2 studies), and 0.16% was parallel concurrent interventional (single study).

Case control studies:

Out of 238 published Case control studies, 95.37% were from Egypt (227 studies), 5 publications from Morocco (350–354), Single case control study was published from each of Sudan (355), Jordan (356), KSA (357), Syria (358), Tunisia (359) and single shared multicenter study between Tunisia, Morocco and Algeria (360).

Four studies (0.66%) describe the epidemiological characteristics of HCC in Arab world, 2 studies from Egypt (361,362), there was single study from Qatar (363) and another single study from KSA (364)

Nineteen studies assessed the different risk factors associated with development, progression and recurrence of HCC. 17 studied were from Egypt and two were from Tunisia.

Another four publications had assessed the incidence of hepatocellular carcinoma (HCC); three publications from Egypt and one from KSA (365).

Only single Arab study assessed the prevalence of HCC among HCV patients in Mid Delta, Egypt (366).

Two Arabian studies discussed the histo-pathological features of HCC, one from Egypt (367) and another from Morocco (367).

There were fourteen studies investigate the role of DNA or RNA in the pathogenesis and gene pathway of HCC. All studies were from Egypt apart of single study from Algeria (368).

There were two studies described the clinical characteristics among patients with HCC. One study from KSA (369), while the second study was from Oman (370).

Three studies evaluate the clinic-pathological features of patients with HCC; 2 studies were from Egypt and one from Tunisia (371).

There were 41 studies reported unusual presentation of hepatocellular carcinoma and metastasis; 36 studies were case reports, single case series from Egypt (372), two cohort studies from Egypt (373), two cross sectional studies ; one from Algeria and another from Tunisia.

Twenty eight Arabian publications evaluated biomarkers that predict early the occurrence of HCC in patients with hepatitis C virus (HCV) induced liver cirrhosis. All studies were from Egypt.

Seven Arabian studies assessed the feasibility and effectiveness of protocols as a screening tool for the detection of early HCC in patients with liver cirrhosis. All studies were from Egypt.

Regarding diagnosis of HCC, there were 228 studies (38.06%) investigated and evaluated the diagnostic performance of multiple serum markers and imaging modalities in diagnosis

prediction and monitoring of HCC. Most of them was from Egypt (95.61%), three from KSA, two studies from Morocco and single study from either of Jordan (356), Sudan, Syria, Tunisia and Bahrain (374).

Ninety-nine studies (16.52%) have discussed the effect of different curative and palliative modalities of HCC on objective response, overall survival, local recurrence and tumor free survival. Most of the studies was from Egypt (88.88%), six studies from KSA, two studies from Lebanon and single study from each of Morocco, Qatar and UAE (375).

Hepatocellular carcinoma (HCC) is a major contributor to the worldwide cancer burden. Incidence rates of HCC have increased in many countries in recent decades (376).

HCC is the seventh-most frequently occurring cancer in the world and the second-most common cause of cancer mortality (377).

There is paucity of publications about incidence and prevalence of HCC in different countries of Arab world. Many research studies are required to detect the incidence and prevalence rates of HCC in Arab world.

Among Arab world, early detection of HCC occurrence is of great clinical value from the diagnostic and prognostic points of view. Review of published screening protocols for early detection of HCC resulted in the need for more and more studies in this important point of research, also we need more research to study and evaluate the efficacy and safety of immune therapies and gene therapy among HCC Arabian patients.

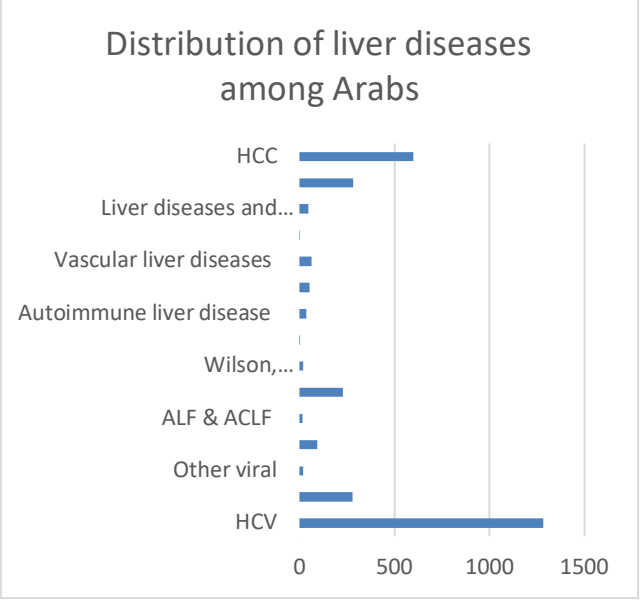

Figure 1: Numbers of publications of each disease title published in Arab world.

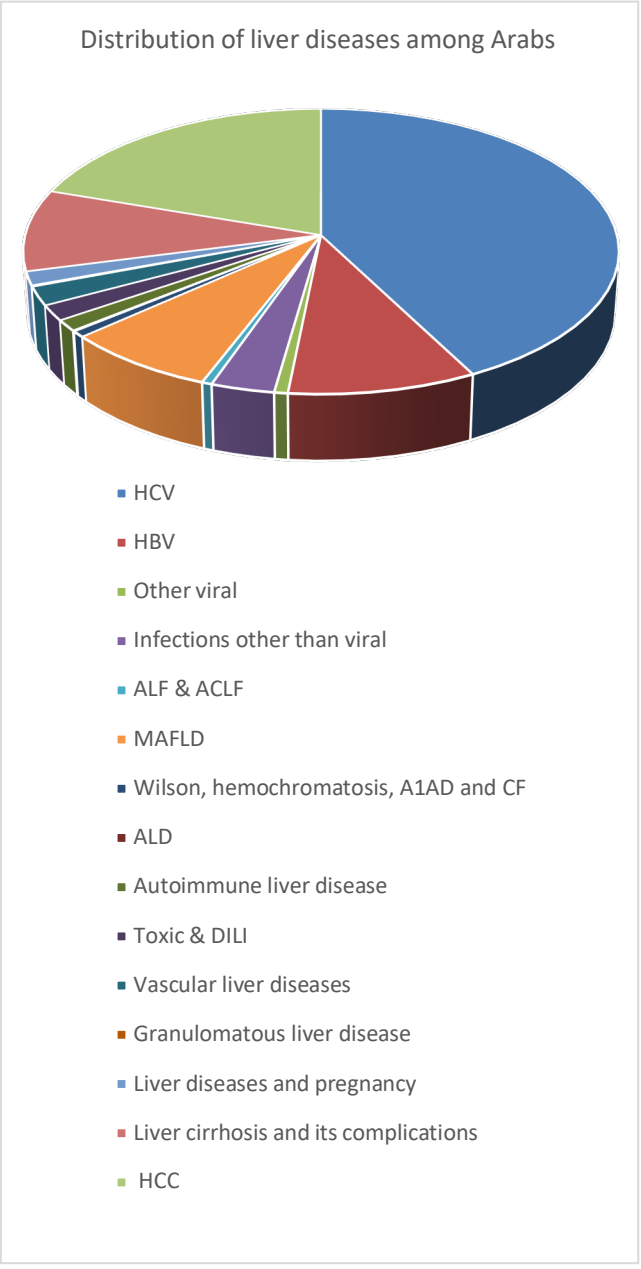

Figure 2: Percentage of publications of each disease title published in Arab world.

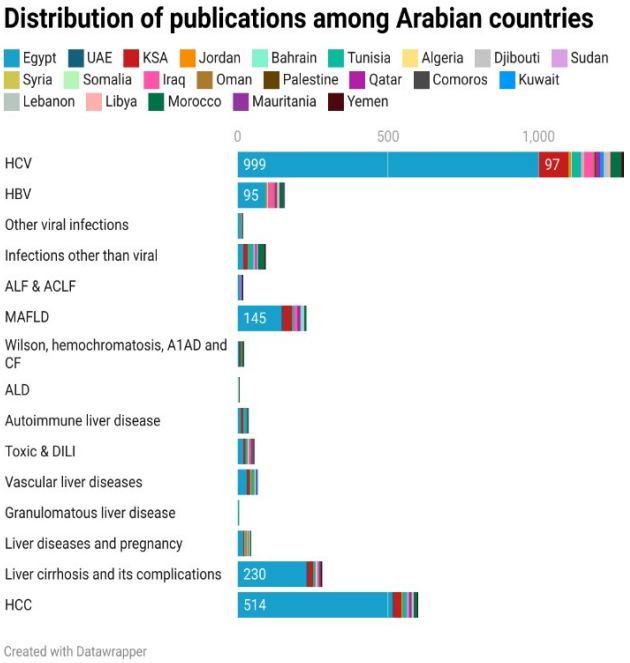

Figure 3: Numbers of publications of each disease title among countries of Arab world.

Declarations: Nothing to declare

R EF ER E N C E S:

1. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol [Internet]. 2019;70(1):151–71. Available from: https://doi.org/10.1016/j.jhep.2018.09.014
2. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: A systematic analysis. BMC Med. 2014;12(1):1–24.
3. Mokdad AH, Forouzanfar MH, Daoud F, Mokdad AA, El Bcheraoui C, Moradi-Lakeh M, et al. Global burden of diseases, injuries, and risk factors for young people's health during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2016;387(10036):2383–401.
4. Klevens RM, Liu S, Roberts H, Jiles RB, Holmberg SD. Estimating acute viral hepatitis infections from nationally reported cases. Am J Public Health. 2014;104(3):482–7.
5. Centers for Disease Control and Prevention (CDC). Viral hepatitis: Surveillance for viral hepatitis. 2018;2018(July):2018.
6. Wang Z, Hu S, Sang S, Luo L, Yu C. Data From the Global Burden of Disease Study 2013. Stroke J Am Hear Assoc. 2017;48(10049):271–6.
7. Kanwal F, Kramer JR, Duan Z, Yu X, White D, El-Serag HB. Trends in the Burden of Nonalcoholic Fatty Liver Disease in a United States Cohort of Veterans. Clin Gastroenterol Hepatol. 2016;14(2):301-308.e2.
8. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73–84.
9. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. Hepatology. 2018;67(1):123–33.
10. Asrani SK, Larson JJ, Yawn B, Therneau TM, Kim WR. Underestimation of liver-related mortality in the United States. Gastroenterology [Internet]. 2013;145(2). Available from: http://dx.doi.org/10.1053/j.gastro.2013.04.005
11. Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: A population-based cohort study. Liver Int. 2012;32(1):79–84.
12. Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020;5(3):245–66.
13. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study Global Burden . JAMA Oncol. 2017;3(4):524–48.
14. Udompap P, Kim D, Kim WR. Current and Future Burden of Chronic Nonmalignant Liver Disease. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2015 Nov;13(12):2031–41.
15. Fidler MM, Bray F. Global cancer inequalities. Front Oncol. 2018;8:293.
16. Alqahtani S, Sanai F, Alolayan A, Abaalkhail F, Alsuhaibani H, Hassanain M, et al. Saudi association for the study of liver diseases and transplantation practice guidelines on the diagnosis and management of hepatocellular carcinoma. Saudi J Gastroenterol. 2020;26(7):S1–40.
17. Fayadh MH. Hepatitis and Liver Diseases. 2016;
18. Blach S, Zeuzem S, Manns M, Altraif I, Duberg AS, Muljono DH, et al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: A modelling study. Lancet Gastroenterol Hepatol. 2017;2(3):161–76.
19. Khan G, Hashim MJ. Burden of virus-associated liver cancer in the Arab world, 1990-2010. Asian Pacific J Cancer Prev. 2015;16(1):265–70.
20. Organization WH. Global hepatitis report 2017. World Health Organization; 2017.
21. Mankoula WAS. Estimating economic and epidemiological burden of hepatitis C in Egypt, 2015-2025. 2015;2015–25.
22. Alboraie M, Youssef N, Sherief AF, Afify S, Wifi MN, Omran D, et al. Egyptian liver library: An indexed database

for liver disease evidence in Egypt. Arab J Gastroenterol [Internet]. 2019;20(2):109–13. Available from: https://doi.org/10.1016/j.ajg.2019.05.004
23. Al-Lawati TT, George M, Al-Lawati FAR. Pattern of liver diseases in Oman. Ann Trop Paediatr. 2009;29(3):183–9.
24. Bassas AF, Chehab MS, Al-shahed MS, Djurberg HG. Pediatric living-related liver. 2002;966(November 2001):640–4.
25. Kagalwalla AF, Al Amir AR, Khalifa A, Sylven M, Al Ajaji S, Kagalwalla YA. Progressive familial intrahepatic cholestasis (Byler's disease) in Arab children. Ann Trop Paediatr. 1995;15(4):321–7.
26. Abdullah AMA, Nazer H, Atiyeh M, Ali MA. Congenital hepatic fibrosis in Saudi Arabia. J Trop Pediatr. 1991;37(5):240–3.
27. Al-Eisa AA, Samhan M, Naseef M. End-stage renal disease in Kuwaiti children: An 8-year experience. Transplant Proc. 2004;36(6):1788–91.
28. Invernizzi P. Geoepidemiology of autoimmune liver diseases. J Autoimmun [Internet]. 2010;34(3):J300–6. Available from: http://dx.doi.org/10.1016/j.jaut.2009.12.002
29. Byass P. The global burden of liver disease: A challenge for methods and for public health. BMC Med. 2014;12(1):1–3.
30. Sepanlou SG, Malekzadeh F, Delavari F, Naghavi M, Forouzanfar MH, Moradi-Lakeh M, et al. Burden of Gastrointestinal and Liver Diseases in Middle East and North Africa: Results of Global Burden of Diseases Study from 1990 to 2010. Middle East J Dig Dis. 2015;7(4):201–15.
31. Swellam M, Mahmoud MS, Ali AAF. Diagnosis of hepatitis C virus infection by enzyme-linked immunosorbent assay and reverse transcriptase-nested polymerase chain reaction: A comparative evaluation. IUBMB Life. 2011;63(6):430–4.
32. Soliman HA, Hozayen WG, Mahmoud AM, Abo-Seif MA, Fayed NA. Significance of the hepatitis C virus core antigen testing as an alternative marker for hepatitis diagnosis in Egyptian patients. Eur Rev Med Pharmacol Sci. 2015;19(12):2240–5.
33. Kamal SM, Kassim S, El Gohary E, Fouad A, Nabegh L, Hafez T, et al. The accuracy and cost-effectiveness of hepatitis C core antigen assay in the monitoring of anti-viral therapy in patients with chronic hepatitis C genotype 4. Aliment Pharmacol Ther. 2015;42(3):307–18.
34. Bartholomeusz A, Locarnini S. Associated With Antiviral Therapy. Antivir Ther. 2006;55(November 2005):52–5.
35. Hassanin TM, Abdelraheem EM, Abdelhameed S, Abdelrazik M, Fouad YM. Detection of hepatitis C virus core antigen as an alternative method for diagnosis of hepatitis C virus infection in blood donors negative for hepatitis C virus antibody. Eur J Gastroenterol Hepatol. 2020;1348–51.
36. El Hadad S, Al-Hamdan H, Linjawi S. Partial sequencing analysis of the NS5B region confirmed the predominance of hepatitis C virus genotype 1 infection in Jeddah, Saudi Arabia. PLoS One. 2017;12(5):1–15.
37. El-Tahan RR, Ghoneim AM, Zaghloul H. 5′ UTR and NS5B-based genotyping of hepatitis C virus in patients from Damietta governorate, Egypt. J Adv Res [Internet]. 2018;10:39–47. Available from: https://doi.org/10.1016/j.jare.2018.01.004
38. Sallam M, Batarseh R, Natsheh A, Abbadi J, Al-Fraihat E, Yaseen A, et al. An update on hepatitis C virus genotype distribution in Jordan: A 12-year retrospective study from a tertiary care teaching hospital in Amman. BMC Infect Dis. 2019;20(1):1–11.
39. Da'as SR, Azzeh M. Subgenotyping and genetic variability of hepatitis C virus in Palestine. PLoS One. 2019;14(10):1–13.
40. Alshaikhly AWAR, Musa ZA, Qasim BJ, Ghazi HF, Mohammed WJ. The distribution of hepatitis c virus genotypes, viral load and antibody titer among iraqi chronic hepatitis patients. Medico-Legal Updat. 2020;20(1):1136–42.
41. Chouikha A, Khedhiri M, Triki H, Hammemi W, Sadraoui A, Touzi H, et al. Focus on hepatitis C virus genotype distribution in Tunisia prior to elimination: a 16-year retrospective study. Arch Virol [Internet]. 2021;166(2):501–10. Available from: https://doi.org/10.1007/s00705-020-04918-7
42. Agha A, Chakik R, Abdulhadi Ali MM, Alsaudi D, Sammito G, Gianninib EG. Peg-interfon alpha-2a and low-dose ribavirin for treatment of hepatitis C virus infection in patients with sickle-cell anemia in Saudi Arabia. Ann Saudi Med. 2013;33(6):610–3.
43. Sanai FM, Mousa D, Al-Mdani A, Al-Shoail G, Al-Ashgar H, Al Meshari K, et al. Safety and efficacy of peginterferon-α2a plus ribavirin treatment in renal transplant recipients with chronic hepatitis C. J Hepatol [Internet]. 2013;58(6):1096–103. Available from: http://dx.doi.org/10.1016/j.jhep.2013.02.004
44. El Naghi S, Abdel-Ghaffar TY, El-Karaksy H, Abdel- Aty EF, El-Raziky MS, Allam AA, et al. Safety and efficacy of Hansenula-derived PEGylated-interferon alpha-2a and ribavirin combination in chronic hepatitis C Egyptian children. World J Gastroenterol. 2014;20(16):4681–91.
45. Mousa N, Besheer T, Gad Y, Elbendary A, Mokbel T, Abdel-Aziz A. Is combination therapy interferon and ribavirin in patients with chronic hepatitis C infection toxic for eyes? J Ocul Pharmacol Ther. 2013;29(3):345–8.
46. Bassiony MM, Yousef A, Youssef U, Salah El-Deen GM, Abdelghani M, Al-Gohari H, et al. Major depressive disorder and generalized anxiety disorder and response to treatment in hepatitis C patients in Egypt. Int J Psychiatry Med. 2015;50(2):147–62.
47. Hafez K, Kamel S, Aal A, Mansour E, Mahran A. The impact of interferon therapy on the sexual function of

hepatitis C male patients. J Curr Med Res Pract. 2019;4(3):319.
48. Doss W, Shiha G, Hassany M, Soliman R, Fouad R, Khairy M, et al. Sofosbuvir plus ribavirin for treating Egyptian patients with hepatitis C genotype 4. J Hepatol [Internet]. 2015;63(3):581–5. Available from: http://dx.doi.org/10.1016/j.jhep.2015.04.023
49. Waked I, Shiha G, Qaqish RB, Esmat G, Yosry A, Hassany M, et al. Ombitasvir, paritaprevir, and ritonavir plus ribavirin for chronic hepatitis C virus genotype 4 infection in Egyptian patients with or without compensated cirrhosis (AGATE-II): a multicentre, phase 3, partly randomised open-label trial. Lancet Gastroenterol Hepatol [Internet]. 2016;1(1):36–44. Available from: http://dx.doi.org/10.1016/S2468-1253(16)30002-4
50. Behairy BE, El-Araby HA, El-Guindi MA, Basiouny HEM, Fouad OA, Ayoub BA, et al. Safety and Efficacy of 8 Weeks Ledipasvir/Sofosbuvir for Chronic Hepatitis C Genotype 4 in Children Aged 4-10 Years. J Pediatr [Internet]. 2020;219:106–10. Available from: https://doi.org/10.1016/j.jpeds.2019.12.034
51. Cordie A, Elsharkawy A, Abdel Alem S, Meshaal S, El Akel W, Abdellatif Z, et al. Sustained virologic response and changes in liver fibrosis parameters following 12-wk administration of generic sofosbuvir and daclatasvir in HIV/HCV-coinfected patients with HCV genotype 4 infection. Trans R Soc Trop Med Hyg. 2020;114(4):232–40.
52. Ragab AboZaid OA, Mahfouz MK, Abdel hammed OM, Maksoud H.A A, Elwan AW, Abdallah OE, et al. Sofosbuvir plus ribavirin combination regimen boost liver functions and antioxidant profile in hepatitis C virus patients. Microb Pathog [Internet]. 2021;150(May 2020):104740. Available from: https://doi.org/10.1016/j.micpath.2021.104740
53. El Kassas M, Alboraie M, El Badry M, Youssef N, Omar H, El Sheemy RY, et al. Retreatment of chronic hepatitis C patients who failed previous therapy with directly acting antivirals: A multicenter study. Int J Infect Dis. 2020;96:367–70.
54. El Kassas M, Alboraie M, Omran D, Salaheldin M, Wifi MN, ElBadry M, et al. An account of the real-life hepatitis C management in a single specialized viral hepatitis treatment centre in Egypt: results of treating 7042 patients with 7 different direct acting antiviral regimens. Expert Rev Gastroenterol Hepatol [Internet]. 2018;12(12):1265–72. Available from: https://doi.org/10.1080/17474124.2018.1476137
55. Dabbous HM, Montasser IF, Sakr MA, Refai R, Sayam M, Abdelmonem A, et al. Safety, efficacy, and tolerability of Sofosbuvir and Ribavirin in management of recurrent hepatitis c virus genotype 4 after living donor liver transplant in Egypt: What have we learned so far? Hepat Mon. 2016;16(5).
56. Ajlan A, Al-Jedai A, Elsiesy H, Alkortas D, Al- Hamoudi W, Alarieh R, et al. Sofosbuvir-based therapy for genotype 4 HCV recurrence post-liver transplant treatment-experienced patients. Can J Gastroenterol Hepatol. 2016;2016.
57. El-Khayat HR, Fouad YM, Maher M, El-Amin H, Muhammed H. Efficacy and safety of sofosbuvir plus simeprevir therapy in Egyptian patients with chronic hepatitis C: A real-world experience. Gut. 2017;66(11):2008–12.
58. Shiha G, Soliman R, ElBasiony M, Hassan AA, Mikhail NNH. Sofosbuvir plus Daclatasvir with or without ribavirin for treatment of chronic HCV genotype 4 patients: real-life experience. Hepatol Int [Internet]. 2018;12(4):339–47. Available from: https://doi.org/10.1007/s12072-018-9861-2
59. Nagaty A, Abd El-Wahab EW. Real-life results of sofosbuvir based therapy in chronic hepatitis C -naïve and -experienced patients in Egypt. PLoS One. 2017;12(10):1–17.
60. Sanai FM, Altraif IH, Alswat K, AlZanbagi A, Babatin MA, AlMousa A, et al. Real life efficacy of ledipasvir/sofosbuvir in hepatitis C genotype 4–infected patients with advanced liver fibrosis and decompensated cirrhosis. J Infect [Internet]. 2018;76(6):536–42. Available from: https://doi.org/10.1016/j.jinf.2018.04.001
61. Elbaz T, Abdo M, Omar H, Hassan EA, Zaghloul AM, Abdel-Samiee M, et al. Efficacy and safety of sofosbuvir and daclatasvir with or without ribavirin in elderly patients with chronic hepatitis C virus infection. J Med Virol. 2019;91(2):272–7.
62. Sarhan II, Ali MM, Abd A, Hassan E. Outcome of Direct Acting Antiviral Drugs (DAADs) for Hepatitis C Virus (HCV) in the Setting of Chronic Kidney Disease (CKD) in Upper Egypt. 2020;81(October):2012–5.
63. Hanafy AS, Soliman S, Abd-Elsalam S. Rescue therapy for chronic hepatitis C virus infection after repeated treatment failures: Impact on disease progression and risk of hepatocellular carcinoma. Hepatol Res. 2019;49(4):377–84.
64. Abdelaziz AO, Nabil MM, Abdelmaksoud AH, Shousha HI, Hashem MB, Hassan EM, et al. Tumor behavior of hepatocellular carcinoma after hepatitis C treatment by direct-acting antivirals: Comparative analysis with non-direct-acting antivirals-treated patients. Eur J Gastroenterol Hepatol. 2019;31(1):75–9.
65. Montasser IF, Ibrahim AA, Farid HM, Al Balakosy AM. De novo hepatocellular carcinoma in cirrhotic hepatitis C virus: Are directly acting antivirals beneficial? Clin Res Hepatol Gastroenterol [Internet]. 2020;101517. Available from: https://doi.org/10.1016/j.clinre.2020.07.022
66. Omar H, El Akel W, Elbaz T, El Kassas M, Elsaeed K, El Shazly H, et al. Generic daclatasvir plus sofosbuvir, with or without ribavirin, in treatment of chronic hepatitis C:

real-world results from 18 378 patients in Egypt. Aliment Pharmacol Ther. 2018;47(3):421–31.
67. Yousif MM, Selim FO, Zedan AM, Samir GM, Fakhr AE. Impact of apo lipoprotein E gene polymorphism on hepatitis C virus disease progression and response to direct acting antivirals in the egyptian population. Hepat Mon. 2020;20(6):1–4.
68. El-Khazragy N, Elshimy AA, Hassan SS, Shaaban MH, Bayoumi AH, El Magdoub HM, et al. lnc-HOTAIR predicts hepatocellular carcinoma in chronic hepatitis C genotype 4 following direct-acting antivirals therapy. Mol Carcinog. 2020;59(12):1382–91.
69. Abdelwahab SF, Hamdy S, Osman AM, Zakaria ZA, Galal I, Sobhy M, et al. Association of the polymorphism of the Toll-like receptor (TLR)-3 and TLR-9 genes with hepatitis C virus- specific cell-mediated immunity outcomes among Egyptian health-care workers. Clin Exp Immunol. 2021;203(1):3–12.
70. Galal GM, Abudeif A, Ahmed NS, Fahmy NF, Sheneef A, Ali EM, et al. Vitamin D receptor gene polymorphisms and risk of hepatocellular carcinoma in hepatitis C-related liver cirrhosis. Egypt Liver J. 2021;11(1):3–11.
71. Fath-Elbab HK, Ahmed E, Mansour DF, Soliman WT. Event-related evoked potential versus clinical tests in assessment of subclinical cognitive impairment in chronic hepatitis C virus. Egypt J Neurol Psychiatry Neurosurg. 2018;54(1):2–7.
72. Elshimi E, Morad W, Mohamad NE. Male Sexual Dysfunction Among Egyptian Patients with Chronic Hepatitis C Virus Infection Before and After Direct-Acting Antiviral Drugs. J Sex Med [Internet]. 2019;16(3):402–9. Available from: https://doi.org/10.1016/j.jsxm.2019.01.309
73. Tawfik YM, Hassany SM, Badran AY, El-Gazzar AF, Alemam MF, Sayed DS. Hepatitis C virus associated skin manifestations in upper Egypt: Before and after direct acting antiviral treatment. Dermatol Ther. 2020;33(6).
74. El-Bendary M, Nour D, Arafa M, Neamatallah M. Methylation of tumour suppressor genes RUNX3, RASSF1A and E-Cadherin in HCV-related liver cirrhosis and hepatocellular carcinoma. Br J Biomed Sci [Internet]. 2020;77(1):35–40. Available from: https://doi.org/10.1080/09674845.2019.1694123
75. Abo El-khair SM, El-Alfy HA, Elsamanoudy AZ, Elhammady D, Abd-elfattah N, Eldeek B, et al. Development of a novel glycated protein-based fibrosis prediction score for determination of significant liver fibrosis in HCV-infected patients, a preliminary study. J Med Virol. 2020;92(12):3525–33.
76. Saleh SA, Salama MM, Alhusseini MM, Mohamed GA. M2BPGi for assessing liver fibrosis in patients with hepatitis C treated with direct-acting antivirals. World J Gastroenterol. 2020;26(21):2864–76.
77. Abd El-Wahab EW, Ayoub HA, Shorbila AA, Mikheal A, Fadl M, Kotkat AM. Noninvasive biomarkers predict improvement in liver fibrosis after successful generic DAAs based therapy of chronic hepatitis C in Egypt. Clin Epidemiol Glob Heal [Internet]. 2020;8(4):1177–88. Available from: https://doi.org/10.1016/j.cegh.2020.04.011
78. Behairy OG, El-Gendy SA, Ibrahim DY, Mansour AI, El-Shimi OS. Mac-2 Binding Protein Glycan Isomer as non-invasive tool to assess liver fibrosis in children with chronic liver disease. Hepatol Res. 2021;(September 2020):277–83.
79. Alboraie M, Khairy M, Elsharkawy A, Elsharkawy M, Asem N, Abo El-Seoud A, et al. Egy-score as a noninvasive score for the assessment of hepatic fibrosis in chronic hepatitis C: A preliminary approach. Saudi J Gastroenterol. 2014;20(3):170–4.
80. Alboraie M, Khairy M, Elsharkawy M, Asem N, Elsharkawy A, Esmat G. Value of Egy-Score in diagnosis of significant, advanced hepatic fibrosis and cirrhosis compared to aspartate aminotransferase-to-platelet ratio index, FIB-4 and Forns' index in chronic hepatitis C virus. Hepatol Res. 2015;45(5):560–70.
81. Alboraie M, Schütte K, Khairy M, Elsharkawy M, Asem N, Elghamry F, et al. Validation of Hepa-index as a non-invasive biomarkers panel for assessment of hepatic fibrosis in Egyptians with chronic hepatitis C. Saudi Med J. 2017;38(11):1137–41.
82. WHO. Interim Guidance For Country Validation of Viral Hepatitis Elimination [Internet]. WHO, Geneva. 2021. 1–96 p. Available from: https://www.who.int/publications/i/item/9789240028395
83. Khaled IAEA, Mahmoud OM, Saleh AF, Bioumie EE. Prevalence of HBV genotypes among Egyptian hepatitis patients. Mol Biol Rep [Internet]. 2011;38(7):4353–7. Available from: https://doi.org/10.1007/s11033-010-0562-8
84. Ismail SA, Cuadros DF, Benova L. Hepatitis B in Egypt: A cross-sectional analysis of prevalence and risk factors for active infection from a nationwide survey. Liver Int [Internet]. 2017 Dec 1;37(12):1814–22. Available from: https://doi.org/10.1111/liv.13469
85. Alzahrani FM, Muzaheed, Shaikh SS, Alomar AI, Acharya S, Elhadi N. Prevalence of Hepatitis B Virus (HBV) among blood donors in eastern Saudi Arabia: Results from a five-year retrospective study of HBV seromarkers. Ann Lab Med. 2018;39(1):81–5.
86. Mursy SMM, Mohamed SOO. Knowledge, attitude, and practice towards Hepatitis B infection among nurses and midwives in two maternity hospitals in Khartoum, Sudan. BMC Public Health [Internet]. 2019;19(1):1597. Available from: https://doi.org/10.1186/s12889-019-7982-8
87. Obeid Charrouf F, Hamze M, Mallat H, Achkar M, Dabboussi F. Characterization of resistance genes in 68 ESBL-producing Klebsiella pneumonia in Lebanon.

Médecine Mal Infect [Internet]. 2014;44(11):535–8. Available from: https://www.sciencedirect.com/science/article/pii/S0399077X14002881
88. Musa SQ, Univversity A, Sabaa S. The prevalence of HCV infections in various groups Of children and adults in central cities of Iraq. 2020;(March).
89. Adouani B, Alami R, Laouina A, Benahadi A, Boulahdid S, Mokhtari A, et al. Hepatitis B in Moroccan blood donors: a decade trend of the HBsAg prevalence in a resources limited country. Transfus Med [Internet]. 2013 Dec 1;23(6):432–7. Available from: https://doi.org/10.1111/tme.12054
90. Al Ashgar H, Peedikayil MC, Al Quaiz M, Al Sohaibani F, Al Fadda A, Khan MQ, et al. HBsAg clearance in chronic hepatitis B patients with add-on pegylated interferon alfa-2a to ongoing tenofovir treatment: A randomized controlled study. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2017;23(3):190–8.
91. Imam MH. The accelerated hepatitis B virus vaccination schedule among hemodialysis patients, does it work? A randomized controlled trial. J Nephrol [Internet]. 2017;30(6):803–9. Available from: https://doi.org/10.1007/s40620-017-0443-5
92. Kitab B, El Feydi AE, Afifi R, Derdabi O, Cherradi Y, Benazzouz M, et al. Hepatitis B genotypes/subgenotypes and MHR variants among Moroccan chronic carriers. J Infect [Internet]. 2011;63(1):66–75. Available from: https://www.sciencedirect.com/science/article/pii/S0163445311003562
93. Al-Qahtani A, Al-Ahdal M, Abdo A, Sanai F, Al-Anazi M, Khalaf N, et al. Toll-like receptor 3 polymorphism and its association with hepatitis B virus infection in Saudi Arabian patients. J Med Virol [Internet]. 2012 Sep 1;84(9):1353–9. Available from: https://doi.org/10.1002/jmv.23271
94. Salama I, Sami S, Saleh R, Mohsen A, Elserougy S, Emam H, et al. Immunogenicity of compulsory and booster doses of hepatitis B vaccine among children in Cairo, Egypt. J Egypt Public Heal Assoc [Internet]. 2017;92(2):77–85. Available from: https://epx.journals.ekb.eg/article_11247.html
95. Khafagy A, AlJahdaly I, Goweda R. Hepatitis B Vaccine: Assessment of Immunologic Response, Coverage Rate, and Factors Influencing Seroreactivity. Clin Lab [Internet]. 2020;66(7). Available from: http://europepmc.org/abstract/MED/32658415
96. Makhlouf NA, Farghaly AM, Zaky S, Rashed H-AG, Abu Faddan NH, Sayed D, et al. The efficacy of hepatitis B vaccination program in upper Egypt: Flow cytometry and the evaluation of long term immunogenicity. J Med Virol [Internet]. 2016 Sep 1;88(9):1567–75. Available from: https://doi.org/10.1002/jmv.24506
97. Darweesh SK, Gad AA, Akroof K, ElLatif ZA. Entecavir and other nucleos(t)ide analogs prophylaxis in hepatitis B virus-related liver transplantation: long-term efficacy and safety [Internet]. Vol. 31, European Journal of Gastroenterology & Hepatology. p. 607–12. Available from: https://www.ingentaconnect.com/content/wk/ejghe/2019/00000031/00000005/art00008
98. Zakaria HM, Salem TA, El-Araby HA, Salama RM, Elbadry DY, Sira AM, et al. Steroid therapy in children with fulminant hepatitis A. J Viral Hepat. 2018;25(7):853–9.
99. BaAlawi F, Hassan K, Al Maamari K, Balkhair A. Fatal hepatitis A virus infection in an adolescent. IDCases. 2020;20:e00721.
100. Ouardani I, Manso CF, Aouni M, Romalde JL. Efficiency of hepatitis A virus removal in six sewage treatment plants from central Tunisia. Appl Microbiol Biotechnol. 2015;99(24):10759–69.
101. Essayagh T, Essayagh M, El Rhaffouli A, Essayagh S. Profil épidémiologique de l'hépatite virale A, Meknès, Maroc, 2013-2016. Med Sante Trop. 2019;29(1):92–6.
102. Qian J-Y, Bai X-Y, Feng Y-L, Zhu W-J, Yao F, Li J-N, et al. Cholestasis, ascites and pancytopenia in an immunocompetent adult with severe cytomegalovirus hepatitis. World J Gastroenterol. 2015;21(43):12505.
103. Obaidat MM, Roess AA. Seroprevalence and risk factors of Hepatitis E infection in Jordan's population: First report. Int J Infect Dis. 2018;66:121–5.
104. Mohiuddin SA, AlMaslamani M, Hashim S, Panthalayinitharayil HK, Alkaabi SR, Abdulwahab A, et al. Measles hepatitis in a vaccinated liver transplant recipient: case report and review of literature. Clin Case Reports. 2017;5(6):867.
105. Farag RMA, AlAyobi D, Alsaleh KA, Kwon H-J, Afaf EL, Dawoud EA. Study the Impact of Cytomegalovirus (CMV) Infection and the Risk Factor for Liver Dysfunction in Saudi Patients. J PurE Appl Microbiol. 2018;12(3):1255–66.
106. El-Gendi AM, El-Shafei M, Bedewy E. The Role of Prophylactic Endoscopic Sphincterotomy for Prevention of Postoperative Bile Leak in Hydatid Liver Disease: A Randomized Controlled Study. J Laparoendosc Adv Surg Tech [Internet]. 2018 Mar 12;28(8):990–6. Available from: https://doi.org/10.1089/lap.2017.0674
107. Daldoul S, Moussi A, Zaouche A. Spontaneous fistulization of hepatic hydatid cyst into the duodenum: An exceptional complication. J Coll Physicians Surg Pakistan. 2013;23(6):424–6.
108. Rami M, Khattala K, Mahmoudi A, Madi AEL, Afifi MA, Bouabdallah Y. Un mode de révélation rare du kyste hydatique hépatique: la rupture intrapéritonéale, à propos de 5 cas. Pan Afr Med J. 2011;8(1).
109. Limeme M, Yahyaoui S, Zaghouani H, Ghannouchi M, Khnissi A, Amara H, et al. Spontaneous intraperitoneal

rupture of hepatic hydatid cyst: a rare cause of ascites. BMC Surg. 2014;14(1):1–4.
110. El Khoury M, El Asmar A, Dib W, Creidi E, Yehia M, Hajj I. Liver hydatid cyst with cutaneous fistulization to the right breast: a case report, management, and literature review. Clin Case Reports. 2017;5(7):1088.
111. En-Nafaa I, Moujahid M, Alahyane A, Amil T, Hanine A, Ziadi T. Hydatid cyst of the liver ruptured into the abdominal wall and the psoas muscle: report of a rare observation. Pan Afr Med J. 2011;10:3.
112. Laalim SA, Toughai I, Oussaden A, Kamaoui I, Mazaz K, Taleb KA. Hydatid cyst of the liver ruptured into the inferior vena cava. Pan Afr Med J. 2011;9:9.
113. Alansari M, Alsanouri I. Atypical intraoperative anaphylactic shock with ECG changes secondary to non-ruptured hepatic hydatid cyst. Case Reports. 2013;2013:bcr2012008442.
114. Albabtain I, Aljohani E, Albrekeit A. ANAPHYLACTIC SHOCK CAUSED BY SPONTANEOUS RUPTURE OF A HEPATIC HYDATID CYST: A CASE REPORT FROM SAUDI ARABIA. INDO Am J Pharm Sci. 2019;6(1):2731–4.
115. Abdelraouf A, El-Aal AAA, Shoeib EY, Attia SS, Hanafy NA, Hassani M, et al. Clinical and serological outcomes with different surgical approaches for human hepatic hydatidosis. Rev Soc Bras Med Trop. 2015;48:587–93.
116. Al-Marzooq TJM, Hassan QA, Alnaser MKH. Ultrasound-guided percutaneous treatment of liver hydatid cysts using 3% hydrogen peroxide as a scolicidal agent: The efficacy and clinical outcomes. Australas Med J. 2017;10(4):285.
117. El-Shabrawi MHF, Bazaraa HM, Zekri H, Rady HI. Fatal acute myocarditis and fulminant hepatic failure in an infant with pandemic human influenza A, H1N1 (2009) virus infection. J Adv Res. 2011;2(2):191–4.
118. El Sayed Zaki M, Othman W. Role of hepatitis E infection in acute on chronic liver failure in Egyptian patients. Liver Int. 2011;31(7):1001–5.
119. Abdel-Ghaffar TY, Sira MM, Sira AM, Salem TA, El-Sharawy AA, El Naghi S. Serological markers of autoimmunity in children with hepatitis A: relation to acute and fulminant presentation. Eur J Gastroenterol Hepatol. 2015;27(10):1161–9.
120. Ayoub B, Ali M, Salem T, Rizk M, Nagi S, Adawy NM. Pediatric chronic liver failure-sequential organ failure assessment score and outcome of acute liver failure in children. Clin Exp Hepatol. 2020;6(3):228–34.
121. Medhat MA, Gushken F, Khaled T, Hassan E, Abd El-Rehim A, Kamel S. Acute-on-chronic liver failure in Egypt: an underestimated complication of liver cirrhosis. Eur J Gastroenterol Hepatol. 2021;33(1S):e458–63.
122. Yadav SK, Gupta RK, Saraswat VA, Rangan M, Thomas MA, Rutella S, et al. Reduced cortical thickness in patients with acute-on-chronic liver failure due to non-alcoholic etiology. J Transl Med. 2015;13(1):1–12.
123. Sayed IM, El-Mokhtar MA, Mahmoud MAR, Elkhawaga AA, Gaber S, Seddek NH, et al. Clinical outcomes and prevalence of hepatitis E virus (HEV) among non-AC hepatitis patients in Egypt. Infect Drug Resist. 2021;14:59.
124. Darweesh SK, Ibrahim MF, El-Tahawy MA. Effect of N-acetylcysteine on mortality and liver transplantation rate in non-acetaminophen-induced acute liver failure: a multicenter study. Clin Drug Investig. 2017;37(5):473–82.
125. AlQassemi ZA, Abd FG. Polymorphism of IL-17 197 A/G in patients with hepatitis B in Iraqi population. Biochem Cell Arch. 2020;20:4195–200.
126. Abusabeib A, El Ansari W, Alobaidan J, Elhag W. First case report of fulminant hepatitis after laparoscopic sleeve gastrectomy associated with concomitant maximal therapeutic dose of acetaminophen use, protein calorie malnutrition, and vitamins A and D, selenium, and glutathione deficiencies. Obes Surg. 2021;31(2):899–903.
127. Fearing MK, Israel EJ, Sahai I, Rapalino O, Lisovsky M. Case 12-2011: A 9-Month-Old Boy with Acute Liver Failure. N Engl J Med. 2011;364(16):1545–56.
128. Husain EH. Fulminant hepatitis in typhoid fever. J Infect Public Health. 2011;4(3):154–6.
129. Hasosah MY, Iskandarani AI, Shawli AI, Alsahafi AF, Sukkar GA, Qurashi MA. Neuroblastoma amplified sequence gene mutation: a rare cause of recurrent liver failure in children. Saudi J Gastroenterol. 2017;23(3):206.
130. Lone KS, AlSaleem B, Asery A, Bashir MS, Al-Hussaini A. Liver failure among young Saudi infants: etiology, clinical presentation, and outcome. J Pediatr Gastroenterol Nutr. 2020;70(2):e26–32.
131. Alswat K, Aljumah AA, Sanai FM, Abaalkhail F, Alghamdi M, Al Hamoudi WK, et al. Nonalcoholic fatty liver disease burden–Saudi Arabia and United Arab Emirates, 2017–2030. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2018;24(4):211.
132. Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology. 2005;41(6):1313–21.
133. Almobarak AO, Barakat S, Khalifa MH, Elhoweris MH, Elhassan TM, Ahmed MH. Non alcoholic fatty liver disease (NAFLD) in a Sudanese population: What is the prevalence and risk factors? Arab J Gastroenterol. 2014;15(1):12–5.
134. Tayyem RF, Al-Dayyat HM, Rayyan YM. Relationship between lifestyle factors and nutritional status and non-alcoholic fatty liver disease among a group of adult Jordanians. Arab J Gastroenterol. 2019;20(1):44–9.
135. Fakhoury-Sayegh N, Younes H, Heraoui GNHA, Sayegh R. Nutritional profile and dietary patterns of lebanese non-alcoholic fatty liver disease patients: a case-control study. Nutrients. 2017;9(11):1245.

136. Borai IH, Shaker Y, Kamal MM, Ezzat WM, Ashour E, Afify M, et al. Evaluation of biomarkers in egyptian patients with different grades of nonalcoholic fatty liver disease. J Clin Transl Hepatol. 2017;5(2):109.
137. Hegazy M, Abo-Elfadl S, Mostafa A, Ibrahim M, Rashed L, Salman A. Serum resistin level and its receptor gene expression in liver biopsy as predictors for the severity of nonalcoholic fatty liver disease. Euroasian J Hepato-Gastroenterology. 2014;4(2):59.
138. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology. 1999;116(6):1413–9.
139. Abdelbasset WK, Elsayed SH, Nambi G, Alrawaili SM, Elnegamy TE, Khalil MA, et al. Effect of moderate-intensity aerobic exercise on hepatic fat content and visceral lipids in hepatic patients with diabesity: a single-blinded randomised controlled trial. Evidence-Based Complement Altern Med. 2020;2020.
140. El-Haggar SM, Mostafa TM. Comparative clinical study between the effect of fenofibrate alone and its combination with pentoxifylline on biochemical parameters and liver stiffness in patients with non-alcoholic fatty liver disease. Hepatol Int. 2015;9(3):471–9.
141. Ismail NA, Mansour NM, Ragab S, Hamed M, Ayoub DF, Elhosary YA. Gut Microbiota Interplay between Obesity and Non Alcoholic Fatty Liver. Res J Pharm Biol Chem Sci. 2015;6(3):1519–28.
142. Algooneh A, Almazeedi S, Al-Sabah S, Ahmed M, Othman F. Non-alcoholic fatty liver disease resolution following sleeve gastrectomy. Surg Endosc. 2016;30(5):1983–7.
143. Usta J, Wehbeh A, Rida K, El-Rifai O, Estiphan TA, Majarian T, et al. Phenotype-genotype correlation in Wilson disease in a large Lebanese family: association of c. 2299insC with hepatic and of p. Ala1003Thr with neurologic phenotype. PLoS One. 2014;9(11):e109727.
144. Altraif I, Handoo FA, Al Ghamdi H, Aljumah A, Al Jumah M, Afzal M. Presentation, diagnosis and outcome of predominantly hepatic Wilson's disease in adult Saudi patients: A single centre experience. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2012;18(5):334.
145. El-Koofy N, Fouad HM, Fahmy ME, Helmy H, Shaker O, El-Karaksy HM, et al. Copper concentrations in Egyptian infants with cholestasis: A single center study. Arab J Gastroenterol. 2018;19(1):21–5.
146. Mahfouz RAR, Sarieddine DS, Charafeddine KM, Abdul Khalik RN, Cortas NK, Daher RT. Should we screen for hereditary hemochromatosis in healthy Lebanese: a pilot study. Mol Biol Rep. 2012;39(1):753–9.
147. Shahin WA, Mehaney DA, El-Falaki MM. Mutation spectrum of Egyptian children with cystic fibrosis. Springerplus. 2016;5(1):1–6.
148. Jouhadi Z, Odou MF, Zerimech F, Bousfiha AA, Mikou N, Porchet N, et al. Alpha1 antitrypsin deficiency due to an homozygous PI* Null Q0Cairo mutation: early onset of pulmonary manifestations and variability of clinical expression. Respir Med case reports. 2018;24:58–62.
149. Tazi I, Nafil H, Boufarissi FZ, Mahmal L. Acanthocytose révélant une cirrhose éthylique. Ann Biol Clin (Paris). 2011;69(6):740–1.
150. Yamamoto T, Friedman SE. Severe Alcohol Withdrawal and Stratification and Management. 2017;(January):38–41.
151. Abdulla AA. Lipid profile and liver enzymes in alcoholic men. Biochem Cell Arch. 2020;20(January):4117–21.
152. Khalifa M, Benjazia E, Rezgui A, Ghannouchi N, Alaoua A, Braham A, et al. Hépatite lupique: une série de 12 patients. Rev Med Interne. 2011;32(6):347–9.
153. Gargouri L, Mnif L, Safi F, Turki F, Majdoub I, Maalej B, et al. Type 2 autoimmune hepatitis overlapping with primary sclerosing cholangitis in a 10-year-old boy. Arch Pediatr [Internet]. 2013;20(12):1325–8. Available from: http://dx.doi.org/10.1016/j.arcped.2013.09.020
154. Masoodi I, Alsayari K. Acute autoimmune hepatitis mimicking metastatic liver disease: A case report. World J Hepatol. 2012;4(7):234–6.
155. Mejri N, Chabchoub I, Gargouri I, Belaid I, Ezairi F, Hmissa S, et al. Effect of chemotherapy on autoimmune hepatitis in thymoma: a case report and literature review. Cancer Biol Med. 2013;10(3):169–73.
156. Salem B, Afef F, Nadia B, Nabil A, Maher B. Portal vein thrombosis in a type 1 autoimmune hepatitis. Pan Afr Med J. 2013;14:2–5.
157. Lalej R, Nadir S, Alaoui R. Maladie coeliaque et hépatite auto-immune de type 2: rapport d'un cas et revue de la littérature. J Africain d'Hepato-Gastroenterologie. 2013;7(4):225–7.
158. Ksouda K, Affes H, Atheymen R, Ezzeddine M, Zeghal K, Hammami S. Autoimmune hepatitis as an adverse effect of long-term methotrexate therapy. Indian J Pharmacol. 2014;46(6):649–50.
159. H Alqrinawi S, Akbar N, Faddag H Al, Akbar S, Akbar L, A S, et al. Menotrophin induced autoimmune hepatitis: a case report. Gastroenterol Hepatol Open Access. 2019;10(3):164–6.
160. Wong F, Al Ibrahim B, Walsh J, Qumosani K. Infliximab-induced autoimmune hepatitis requiring liver transplantation. Clin Case Reports [Internet]. 2019 Nov 1;7(11):2135–9. Available from: https://doi.org/10.1002/ccr3.2456
161. Tharwat S, Eltoraby EE. Pyodermatitis-pyostomatitis vegetans associated with autoimmune hepatitis: unreported co-existence. Gastroenterol Hepatol from bed to bench [Internet]. 2020;13(2):188–90. Available from:

http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm&NEWS=N&AN=32308944
162. Abu Faddan NH, Abdel-Baky L, Aly SA, Rashed H allah G. Clinico-laboratory study on children with auto-immune hepatitis in Upper Egypt. Arab J Gastroenterol [Internet]. 2011;12(4):178–83. Available from: http://dx.doi.org/10.1016/j.ajg.2011.11.003
163. El-Shabrawi M, El-Karaksy H, Mohsen N, Isa M, Al-Biltagi M, El-Ansari M. Celiac disease in children and adolescents with autoimmune hepatitis: A single-centre experience. J Trop Pediatr. 2011;57(2):104–8.
164. Al-Hussaini AA, Alzahrani MD, Alenizi AS, Suliman NM, Khan MA, Alharbi SA, et al. Autoimmune hepatitis related autoantibodies in children with type 1 diabetes. Diabetol Metab Syndr. 2014;6(1):2–6.
165. Behairy BE, El-Araby HA, Abd El Kader HH, Ehsan NA, Salem ME, Zakaria HM, et al. Assessment of intrahepatic regulatory T cells in children with autoimmune hepatitis. Ann Hepatol. 2016;15(5):682–90.
166. Behairy OGA. Characteristics of autoimmune hepatitis in a sample of Egyptian children. Egypt Pediatr Assoc Gaz [Internet]. 2017;65(4):108–13. Available from: https://doi.org/10.1016/j.epag.2017.11.002
167. Saadah OI, Khayat A, Alsufyani HA, Bin-Taleb Y. Paediatric autoimmune liver diseases: A descriptive study of patients from Saudi Arabia. Arab J Gastroenterol [Internet]. 2021;22(2):146–50. Available from: https://doi.org/10.1016/j.ajg.2021.05.009
168. Farid E, Isa HM, Nasef M Al, Mohamed R. Childhood Autoimmune Hepatitis in Bahrain: a Tertiary Center Experience. 2015;
169. Fallatah HI, Akbar HO. Autoimmune liver disease - are there spectra that we do not know? Comp Hepatol. 2011;10:1–7.
170. Lahcene M, Oumnia N, Chiali N, Benzaghou L. Hépatites auto-immunes de l'adulte. Expérience d'un service de médecine interne algérien. J Africain d'Hepato-Gastroenterologie. 2013;7(4):220–4.
171. Abdel-Razik A, Mousa N, Zakaria S, Elhelaly R, Elzehery R, Zalata K, et al. New predictive factors of poor response to therapy in autoimmune hepatitis: Role of mean platelet volume. Eur J Gastroenterol Hepatol. 2017;29(12):1373–9.
172. Chaouali M, Carvalho A, Tezeghdenti A, Ben Azaiez M, Cunha C, Ghazouani E, et al. Cytotoxic T lymphocyte antigen-4 gene polymorphisms and susceptibility to type 1 autoimmune hepatitis in the Tunisian population. Genes Dis [Internet]. 2018;5(3):256–62. Available from: https://doi.org/10.1016/j.gendis.2017.12.006
173. Zgair AK. Involvement of (IgG and IgM)-secreting B lymphocytes in severity of autoimmune hepatitis type 1. Med Microbiol Immunol. 2013;202(3):229–37.
174. Behairy OG, Behiry EG, El Defrawy MS, El Adly AN. Diagnostic value of soluble programmed cell death protein-1 in type-1 autoimmune hepatitis in Egyptian children. Scand J Clin Lab Invest [Internet]. 2020;80(1):59–65. Available from: https://doi.org/10.1080/00365513.2019.1695283
175. Chaouali M, Azaiez M Ben, Tezeghdenti A, Yacoubi-Oueslati B, Ghazouani E, Kochkar R. High levels of proinflammatory cytokines IL-6, IL-8, TNF-A, IL-23, and IFN-γ in Tunisian patients with type 1 autoimmune hepatitis. Eur Cytokine Netw. 2020;31(3):94–103.
176. Ibn Sellam A, Gharbaoui Y, Rhorfi-Abderrahmani I, Asbaai EH, Rguibi-Idrissi M, Abid A, et al. Pneumonie organisée associée à une cirrhose biliaire primitive. Rev Mal Respir. 2011;28(9):1167–71.
177. Kharrasse G, Errabih I, Krami HE, Benzzoubeir N, Ouazzani L, Jahid A, et al. Association cirrhose biliaire primitive et maladie de Biermer. À propos d'une nouvelle observation. J Africain d'Hepato-Gastroenterologie. 2011;5(1):46–50.
178. Sultan K, Petkar M, Derbala M. Florid biliary duct lesions in an AMA -positive patient in absence of cholestatic liver biochemistry. J Autoimmun [Internet]. 2019;101(February):153–5. Available from: https://doi.org/10.1016/j.jaut.2019.04.004
179. Ghorbel I Ben, Feki NB, Salem T Ben, Hamzaoui A, Khanfir M, Lamloum M, et al. of Kidney Diseases and Transplantation Case Report Microscopic Polyangiitis Associated with Primary Biliary Cirrhosis , Sjo gren ' s S yndrome and Hashimoto ' s Thyroiditis. 2015;26(2):359–62.
180. Eid M, Matrawy KA. Primary sclerosing cholangitis: Evaluation with MR cholangiopancreatography (MRCP). Egypt J Radiol Nucl Med [Internet]. 2011;42(3–4):351–6. Available from: http://dx.doi.org/10.1016/j.ejrnm.2011.09.007
181. Sabib M, Ettair S, Erreimi N, Mouane N. [Sclerosing cholangitis revealing Langerhans cell histiocytosis in a 15-month-old child]. Arch pédiatrie organe Off la Sociéte Fr pédiatrie [Internet]. 2011;18(9):974–8. Available from: http://www.sciencedirect.com/science/article/pii/S0929693X11002806
182. Majid N, Bernoussi Z, Mrabti H, Errihani H. Celiac Disease, Enteropathy-Associated T-Cell Lymphoma, and Primary Sclerosing Cholangitis in One Patient: A Very Rare Association and Review of the Literature. Case Rep Oncol Med. 2013;2013:1–3.
183. Al Salloom AA, Almalki ST, AlMana H. Diabetes Insipidus and Sclerosing Cholangitis in a Child May Be a Clue to the Diagnosis of Langerhans' Cell Histiocytosis : A Case Report. Int J Health Sci (Qassim). 2013;7(2):248–51.
184. Tfifha M, Kamoun T, Mama N, Mestiri S, Hassayoun S, Zouari N, et al. Childhood sclerosing cholangitis associations in a tunisian tertiary care hospital: A many-faceted disease. Turk J Pediatr. 2019;61(6):905–14.

185. Varghese G, Madi L, Ghannam M, Saad R. A possible increase in liver enzymes due to amlodipine: A case report. SAGE Open Med Case Reports. 2020;8:2050313X2091782.
186. Ben-Nasr H, Ksouda K, Harrabi B, Hammami ST, Zeghal K, Affes H. Pediatric liver failure following mefenamic acid associated to herbal auto-medication: A case report. Vol. 74, Therapie. France; 2019. p. 677–80.
187. Al-Sinani S, Al-Rawas A, Dhawan A. Mercury as a cause of fulminant hepatic failure in a child: Case report and literature review. Clin Res Hepatol Gastroenterol [Internet]. 2011;35(8–9):580–2. Available from: http://dx.doi.org/10.1016/j.clinre.2011.06.006
188. Ben Fredj N, Chaabane A, Chadly Z, Ben Fadhel N, Boughattas NA, Aouam K. Albendazole-induced associated acute hepatitis and bicytopenia. Scand J Infect Dis. 2014;46(2):149–51.
189. Seife Hassen S, Ata F, Bint I Bilal A, Salih Ali M, Petkar M, Awad Elzouki AY, et al. Immune-mediated drug-induced liver injury secondary to Omeprazole: A case report. Clin Case Reports [Internet]. 2020 Dec 1;8(12):3420–5. Available from: https://doi.org/10.1002/ccr3.3421
190. Hagag AA, Elgamsy MA, El-Asy HM, Mabrouk MM. Protective role of silymarin on hepatic and renal toxicity induced by MTX based chemotherapy in children with acute lymphoblastic leukemia. Mediterr J Hematol Infect Dis. 2016;8(1):1–9.
191. Hasanain AFA, Zayed AA-AH, Mahdy RE, Nafee AMA. Cholecalciferol for prophylaxis against antituberculosis therapy-induced liver disorders among naïve patients with pulmonary tuberculosis: A randomized, comparative study. Int J mycobacteriology. 2017;6(2):149.
192. Maier-Salamon A, Elgendy SA, Meyer B, Vossen M, Thalhammer T, Thalhammer F, et al. Pharmacokinetics of flucloxacillin and its metabolites in patients with renal failure: Impact on liver toxicity. Int J Clin Pharmacol Ther. 2017;55(9):701–11.
193. Canguven O, Talib RA, El Ansari W, Yassin DJ, Salman M, Al-Ansari A. Testosterone therapy has positive effects on anthropometric measures, metabolic syndrome components (obesity, lipid profile, Diabetes Mellitus control), blood indices, liver enzymes, and prostate health indicators in elderly hypogonadal men. Andrologia. 2017;49(10):1–6.
194. Abd-Allah SS, El-Morsy A, El-Badrawy A, Settein M, El-Etreby S, Halim A, et al. Multi-detector computed tomography (MDCT) findings of chemotherapy induced hepatic changes. Egypt J Radiol Nucl Med [Internet]. 2016;47(3):693–8. Available from: http://dx.doi.org/10.1016/j.ejrnm.2016.05.007
195. Sridharan K, Daylami A Al, Ajjawi R, Ajooz HAMA. Drug-Induced Liver Injury in Critically Ill Children Taking Antiepileptic Drugs: A Retrospective Study. Curr Ther Res - Clin Exp [Internet]. 2020;92:100580. Available from: https://doi.org/10.1016/j.curtheres.2020.100580
196. Devarbhavi H, Raj S, Aradya VH, Rangegowda VT, Veeranna GP, Singh R, et al. Drug-induced liver injury associated with stevens-Johnson syndrome/toxic epidermal necrolysis: Patient characteristics, causes, and outcome in 36 cases. Hepatology [Internet]. 2016 Mar 1;63(3):993–9. Available from: https://doi.org/10.1002/hep.28270
197. Mevada ST, AlDhuli AS, Al-Rawas AH, Al-Khabori MK, Nazir H, Zachariah M, et al. Liver Enzymes Changes and Safety Profile of Deferasirox Iron Chelator in Omani Children with Thalassemia Major. Blood [Internet]. 2014;124(21):4903–4903. Available from: http://dx.doi.org/10.1182/blood.V124.21.4903.4903
198. Alkharfy TM, Ba-Abbad R, Hadi A, Sobaih BH, AlFaleh KM. Total parenteral nutrition-associated cholestasis and risk factors in preterm infants. Saudi J Gastroenterol. 2014;20(5):293–6.
199. Khalife M, Faraj W, Salah F, Haydar AA. Congestive hepatopathy secondary to large renal arteriovenous malformation. Case Reports. 2013;2013:bcr2012007818.
200. El-Assaly H, Metwally LIA, Azzam H, Seif-Elnasr MI. A comparative study of multi-detector CT portography versus endoscopy in evaluation of gastro-esophageal varices in portal hypertension patients. Egypt J Radiol Nucl Med. 2020;51(1):1–10.
201. Mubarak AA, Awad GE, Eltomey MA, Dawoud MAE. Non-contrast MR portography using time-spatial labeling inversion pulse for diagnosis of portal vein pathology. Egypt J Radiol Nucl Med. 2019;50(1):1–8.
202. Kamaoui I, Maaroufi M, Oussaden A, Abid H, Boubou M, Houssaini NS, et al. Varices grêliques: intérêt de l'angioscanner abdominal. J Radiol. 2011;92(10):933–5.
203. Elleuch N, Sabbek A, Hammami A, Ksiaa M, Jmaa A. Primary peritoneal tuberculosis, a forgotten etiology of portal vein thrombosis. J Med Vasc. 2020;45(2):96–8.
204. Alsayid M, Abdulbaki R, Alkharrat R, Alsabbagh MEY. Isolated Spontaneous Hepatic Artery Dissection: A Case Report: 1988. Off J Am Coll Gastroenterol ACG. 2016;111:S948.
205. Ennaifer R, Bacha D, Romdhane H, Cheikh M, Nejma H Ben, BelHadj N. Budd-Chiari syndrome: an unusual presentation of multisystemic sarcoidosis. Clin Pract. 2015;5(3):768.
206. Afredj N, Guessab N, Nani A, Faraoun SA, Cheikh IO, Kerbouche R, et al. Aetiological factors of Budd-Chiari syndrome in Algeria. World J Hepatol. 2015;7(6):903.
207. Ghaffar TYA, Elsayed SM, Sakr MA, Elsobky ES, Abdelhakam SM, Yousuf S, et al. Factor V G1691A (Leiden) is a major etiological factor in Egyptian Budd-Chiari syndrome patients. Turkish J Hematol. 2011;
208. Sakr M, Barakat E, Abdelhakam S, Dabbous H, Yousuf S, Shaker M, et al. Epidemiological aspects of Budd-Chiari in Egyptian patients: a single-center study. World J Gastroenterol WJG. 2011;17(42):4704.

209. Eldorry A, Barakat E, Abdella H, Abdelhakam S, Shaker M, Hamed A, et al. Outcome of non surgical hepatic decompression procedures in Egyptian patients with Budd-Chiari. World J Gastroenterol WJG. 2011;17(7):906.
210. Gawish E, Abd El-Monem E, El-Abd M, Sobhy GA, Ghanem H. MicroRNA-499 rs3746444 polymorphism in Egyptian children with biliary atresia. Clin Exp Hepatol. 2020;6(3):263–9.
211. Abdallah M, Généreau T, Donadieu J, Emile J-F, Chazouillères O, Gaujoux-Viala C, et al. Langerhans' cell histiocytosis of the liver in adults. Clin Res Hepatol Gastroenterol [Internet]. 2011;35(6):475–81. Available from: https://www.sciencedirect.com/science/article/pii/S2210740111001240
212. Moussa M, Abou Chakra M. Granulomatous hepatitis caused by Bacillus Calmette-Guerin (BCG) infection after BCG bladder instillation: A case report. Vol. 20, Urology case reports. United States; 2018. p. 3–4.
213. Azzaza M, Farhat W, Ammar H, Mizouni A, Said MA, Harrabi F, et al. Isolated hepatic tuberculosis presenting as hydatid cyst. Clin J Gastroenterol [Internet]. 2020;13(3):408–12. Available from: https://doi.org/10.1007/s12328-019-01071-w
214. Alsaif HS, Hassan A, Refai O, Awary K, Kussaibi H, Ismail MH, et al. Concomitant hepatic tuberculosis and hepatocellular carcinoma: a case report and review of the literature. BMC Surg [Internet]. 2021;21(1):2. Available from: https://doi.org/10.1186/s12893-020-01021-1
215. Coash M, Forouhar F, Wu CH, Wu GY. Granulomatous liver diseases: A review. J Formos Med Assoc [Internet]. 2012;111(1):3–13. Available from: https://www.sciencedirect.com/science/article/pii/S0929664612000034
216. Ishak KG, Zimmerman HJ. 11 Drug-induced and toxic granulomatous hepatitis. Baillieres Clin Gastroenterol [Internet]. 1988;2(2):463–80. Available from: https://www.sciencedirect.com/science/article/pii/0950352888900127
217. Othman B, Al-Najjar MAA, Othman D, Al-Qudah R, Basheti I. Prevalence, knowledge of and attitude towards hepatitis B virus among pregnant females in Jordan. J Viral Hepat. 2020;27(11):1108–18.
218. Al-Essa M, Alyahya A, Al Mulhim A, Alyousof A, Al-Mulhim M, Essa A. Perception of and attitude towards hepatitis B infection among Saudi pregnant females attending antenatal care unit in Al-Ahsa City, Kingdom of Saudi Arabia. Cureus. 2020;12(1).
219. Kishk R, Mandour M, Elprince M, Salem A, Nemr N, Eida M, et al. Pattern and interpretation of hepatitis B virus markers among pregnant women in North East Egypt. Brazilian J Microbiol [Internet]. 2020;51(2):593–600. Available from: https://doi.org/10.1007/s42770-019-00174-3
220. Elkheir SM, Babiker ZOE, Elamin SK, Yassin MIA, Awadalla KE, Bealy MA, et al. Seroprevalence of maternal HIV, hepatitis B, and syphilis in a major maternity hospital in North Kordofan, Sudan. Int J STD AIDS [Internet]. 2018 Jul 27;29(13):1330–6. Available from: https://doi.org/10.1177/0956462418784687
221. Ahmed MA, Sharif ME, Rayis DA, Nasr AM, Adam I. Hepatitis B infection and preeclampsia among pregnant Sudanese women. Virol J [Internet]. 2018;15(1):20. Available from: https://doi.org/10.1186/s12985-018-0927-5
222. Mudardum AH, Mohammed AA. Prevalence and risk factors for hepatitis B infection among pregnant women attending antenatal clinic in UM dafog area, South Darfur state, Sudan. Sudan J Med Sci. 2019;14(3):116–25.
223. Murad EA, Babiker SM, Gasim GI, Rayis DA, Adam I. Epidemiology of hepatitis B and hepatitis C virus infections in pregnant women in Sana'a, Yemen. BMC Pregnancy Childbirth [Internet]. 2013;13(1):127. Available from: https://doi.org/10.1186/1471-2393-13-127
224. Elsheikh RM, Daak AA, Elsheikh MA, Karsany MS, Adam I. Hepatitis B virus and hepatitis C virus in pregnant Sudanese women. Virol J [Internet]. 2007;4(1):104. Available from: https://doi.org/10.1186/1743-422X-4-104
225. Basha A, Amarin Z, Haloub K, Kharabsheh A, Qudah O, Abu-Khader I. Epidemiology of hepatitis B and C in a pregnant woman in a tertiary teaching hospital in Jordan. CEOG. 2019;46(5):723–6.
226. Mostafa A, Ebeid FSE, Khaled B, Ahmed RHM, El-Sayed MH. Micro-elimination of hepatitis C through testing of Egyptian pregnant women presenting at delivery: implications for screening policies. Trop Med Int Heal. 2020;25(7):850–60.
227. Al-Kubaisy W, Daud S, Al-Kubaisi MW, Al-Kubaisi OW, Abdullah NN. Maternal hepatitis C (HCV) infection and Anti-D immunoglobulin therapy: study testing antibodies, RNA and Genotype of HCV in Baghdad. J Matern Neonatal Med. 2019;32(20):3464–9.
228. Rezk M, Omar Z. Deleterious impact of maternal hepatitis-C viral infection on maternal and fetal outcome: a 5-year prospective study. Arch Gynecol Obstet. 2017;296(6):1097–102.
229. Ismail MB, Khodor S, Osman M, Mallat H, Dabboussi F, Hamze M. Seroprevalence of hepatitis E virus in pregnant women in northern Lebanon. East Mediterr Heal J. 2020;26(5):580–5.
230. Rayis DA, Jumaa AM, Gasim GI, Karsany MS, Adam I. An outbreak of hepatitis E and high maternal mortality at Port Sudan, Eastern Sudan. Pathog Glob Health. 2013;107(2):66–8.
231. Hannachi N, Hidar S, Harrabi I, Mhalla S, Marzouk M, Ghzel H, et al. Seroprevalence and risk factors of hepatitis

E among pregnant women in central Tunisia. Pathol Biol (Paris). 2009;59(5):e115-8.
232. Yassin A, Denguezli W, Fessi A, Njim L, Falah R, Zakhama A, et al. Mild clinical presentation of acute fatty liver in the second trimester of pregnancy. Case Rep Obstet Gynecol. 2011;2011.
233. Al Riyami N, Al-Harthy A, Zia F. Atypical case of acute Fatty liver of pregnancy. Sultan Qaboos Univ Med J. 2011;11(4):507.
234. Masoodi I, Al-Lehibi A, Wani A, Alqutub A. Acute fatty liver of pregnancy mimicking puerperal sepsis: Report of a case with literature review. Saudi J Med Med Sci. 2016;4(1):42.
235. Al-Husban N, Al-Kuran O, Al Helou A. Postpartum acute fatty liver of pregnancy: a case report. J Med Case Rep. 2018;12(1):1–6.
236. Ramadan MK, Khaza'al J, Cha'ar D, Bazzi Z, Bachnak R, Haibeh P. Second-trimester acute fatty liver disease of pregnancy: a brief review of the literature and a case report. J Obstet Gynaecol Res. 2021;47(1):34–43.
237. Rachidi K, Omari D. Acute fatty liver of pregnancy with right acute pyelonephritis on a twin pregnancy: a rare combination. Pan Afr Med J. 2013;15:151.
238. Doumiri M, Elombila M, Oudghiri N, Saoud AT. Ruptured subcapsular hematoma of the liver complicating acute fatty liver of pregnancy. Pan Afr Med J. 2014;19:38.
239. Mellouli MM, Amara F Ben, Maghrebi H, Bouchnack M, Khaled N, Reziga H. Acute fatty liver of pregnancy over a 10-year period at a Tunisian tertiary care center. Int J Gynaecol Obstet. 2012;117(1):88–9.
240. Al Shobaili HA, Hamed HO, Al Robaee A, Alzolibani AA, Amin AF, Ahmad SR. Obstetrical and fetal outcomes of a new management strategy in patients with intra-hepatic cholestasis of pregnancy. Arch Gynecol Obstet. 2011;283(6):1219–25.
241. Ataalla WM, Ziada DH, Gaber R, Ossman A, Bayomy S, Elemary BR. The impact of total bile acid levels on fetal cardiac function in intrahepatic cholestasis of pregnancy using fetal echocardiography: a tissue Doppler imaging study. J Matern Neonatal Med. 2016;29(9):1445–50.
242. Salame AA, Jaffal MJ, Mouanness MA, Nasser Eddin AR, Ghulmiyyah LM. Unexplained first trimester intrahepatic cholestasis of pregnancy: a case report and literature review. Case Rep Obstet Gynecol. 2019;2019.
243. Abdalla MS. Correlations of complete blood count, liver enzyme and serum uric Acid in Sudanese pre-eclamptic cases. 2018;
244. El-Gamal RA, Mekawy MA, Abd Elkader AM, Abdelbary HM, Fayek MZ. Combined immature platelet fraction and schistocyte count to differentiate pregnancy-associated thrombotic thrombocytopenic purpura from severe preeclampsia/haemolysis, elevated liver enzymes, and low platelet syndrome (SPE/HELLP). Indian J Hematol Blood Transfus. 2020;36(2):316–23.
245. Elkhateb IT, Mousa A, Hashem A. Budd-Chiari syndrome diagnosed with pregnancy in a patient with inherited thrombophilia. BMJ Case Reports CP. 2021;14(1):e237761.
246. Rasheed SM, Monem AMA, Abd Ellah AH, Fattah MSA. Prognosis and determinants of pregnancy outcome among patients with post-hepatitis liver cirrhosis. Int J Gynecol Obstet. 2013;121(3):247–51.
247. Elsiesy H, Saad M, Shorman M, Amr S, Abaalkhail F, Hashim A, et al. Invasive mucormycosis in a patient with liver cirrhosis: case report and review of the literature. Hepat Mon. 2013;13(8).
248. ALLAM AS, ANWAR AG, GHAIT RS, ABDEL RAHMAN T, KABIEL WAY, NASSER HM, et al. A NON INVASIVE METHOD FOR DIAGNOSIS AND ASSESSMENT OF PORTAL HYPERTENSION IN EGYPTIAN CIRRHOTIC PATIENTS USING PLASMA MALONDIALDEHYDE LEVEL. J Egypt Soc Parasitol. 2019;49(3):661–8.
249. Baz AAM, Mohamed RM, El-kaffas KH. Doppler ultrasound in liver cirrhosis: correlation of hepatic artery and portal vein measurements with model for end-stage liver disease score in Egypt. Egypt J Radiol Nucl Med. 2020;51(1):1–10.
250. Elwan N, Salah R, Hamisa M, Shady E, Hawash N, Abd-Elsalam S. Evaluation of portal pressure by doppler ultrasound in patients with cirrhosis before and after simvastatin administration–a randomized controlled trial. F1000Research. 2018;7.
251. Seif HMAH, Rahma MZA, Zaky S, Swifee YM. Transjugular intrahepatic porto-systemic shunt in bleeding esophageal varices and refractory ascites. The first 4 years experience in Assiut University Hospital. Egypt J Radiol Nucl Med. 2016;47(3):825–32.
252. Alwarraky MS, Elzohary HA, Melegy MA, Mohamed A. Stent patency and outcome of TIPS through the left versus the right portal branches. Egypt J Radiol Nucl Med. 2020;51(1):1–9.
253. Zaky S, Fouad EA, Kotb HIM. The effect of rectal ozone on the portal vein oxygenation and pharmacokinetics of propranolol in liver cirrhosis (a preliminary human study). Br J Clin Pharmacol. 2011;71(3):411–5.
254. El Shahawy MS, Shady ZM, Gaafar A. The efficacy of argon plasma coagulation versus carvedilol for treatment of portal hypertensive gastropathy. Digestion. 2020;101(6):651–8.
255. Mohiuddin SA, Sharma M, Thandassery RB, Al Mohannadi M, Yacoob R, Muzrakchi A, et al. Large fundal varices: to glue or not to glue? Ann Gastroenterol. 2014;434.
256. Ahmed R, Kiyosue H, Mori H, Abdelaziz S, Othman M, Abdel-Aal S, et al. Conventional versus selective balloon-occluded retrograde transvenous obliteration of gastric varices. Egypt J Radiol Nucl Med. 2020;51(1):1–11.

257. Seleem WM, Hanafy AS. Management of different types of gastric varices with band ligation: a 3-year experience. Eur J Gastroenterol Hepatol. 2017;29(8):968–72.
258. Elwakil R, Montasser MF, Abdelhakam SM, Ibrahim WA. N-butyl-2-cyanoacrylate, iso-amyl-2-cyanoacrylate and hypertonic glucose with 72% chromated glycerin in gastric varices. World J Gastrointest Endosc. 2015;7(4):411.
259. Gabr MM. 1157 Under Water Injection of Fundal Varices. Gastrointest Endosc. 2017;85(5):AB158.
260. Dessouky BAM. Multidetector CT oesophagography: An alternative screening method for endoscopic diagnosis of oesophageal varices and bleeding risk. Arab J Gastroenterol. 2013;14(3):99–108.
261. Nada L, El Fakir S, Bahija B, Adil I, Nourdine A. Noninvasive predictors of presence and grade of esophageal varices in viral cirrhotic patients. Pan Afr Med J. 2015;20(1).
262. Elalfy H, Elsherbiny W, Rahman AA, Elhammady D, Shaltout SW, Elsamanoudy AZ, et al. Diagnostic non-invasive model of large risky esophageal varices in cirrhotic hepatitis C virus patients. World J Hepatol. 2016;8(24):1028.
263. Mahfouz H, Fakhry M, Afifi M, Nafady M, Amer K, El-shamy A, et al. Detection of risky esophageal varices by two-dimensional ultrasound: when to perform endoscopy. Am J Med Sci. 2014;347(1):28–33.
264. Sobhey OM, Jouda AA, Metwally A, Shawky NM, Elkhashab MN. Evaluation of serum kallistatin level as a predictor of esophageal varices in cirrhotic patients. Alexandria J Med. 2020;56(1):21–6.
265. Elkenawy YN, Elarabawy RA, Ahmed LM, Elsawy AA. Portal vein flow velocity as a possible fast noninvasive screening tool for esophageal varices in cirrhotic patients. JGH Open. 2020;4(4):589–94.
266. Salman A, Salman MA, Ismaeel Saadawy AM, Tourky M, Shawkat M. Portal venous hemodynamics as predictors for the development and grades of esophageal varices in Post-HCV cirrhotic patients: An Egyptian center study. Adv Dig Med. 2021;8(3):146–54.
267. Darweesh SK, Elsabaawy MA, Eltahawy MA, Ghanem HS, Abdel-Razek W. Serum ammonia as a non-invasive marker for early prediction of esophageal varices. Eur J Gastroenterol Hepatol. 2021;32(2):230–6.
268. Fouad TR, Abdelsameea E, Abdel-Razek W, Attia A, Mohamed A, Metwally K, et al. Upper gastrointestinal bleeding in Egyptian patients with cirrhosis: Post-therapeutic outcome and prognostic indicators. J Gastroenterol Hepatol. 2019;34(9):1604–10.
269. Naga M, Wahba M, Okasha H, Farag A, El-Mazny A, Elbadri A, et al. Comparative study of tissue adhesive therapy versus band ligation in control of actively bleeding esophageal varices. Acta Gastroenterol Belg. 2020;83.
270. Kassim A, Ameen S, Musead M. Non-Invasive Assessment of Esophageal Varices in Cirrhotic Yemeni Patients. Int J Med Res Heal Sci. 2018;7(7):119–26.
271. Wasfy E, Elkassas G, Elnawasany S, Elkasrawy K, Abd-Elsalam S, Soliman S, et al. Predicting esophageal varices in cirrhotic hepatitis C virus patients using noninvasive measurement of insulin resistance variables. Endocrine, Metab Immune Disord Targets (Formerly Curr Drug Targets-Immune, Endocr Metab Disord. 2018;18(6):573–80.
272. Ellakany WI, Mahmoud MoheyEldin K, Invernizzi P, Mahmoud ElKady A, Eldin Fathy Abou Elkheir H, Abdel Haleem Abo Elwafa R, et al. Study of the influence of heme oxygenase 1 gene single nucleotide polymorphism (rs2071746) on esophageal varices among patients with cirrhosis. Eur J Gastroenterol Hepatol. 2018;30(8):888–92.
273. Salman AA, Shaaban HED, Atallah M, Yousef M, Ahmed RA, Ashoush O, et al. Long-term outcome after endoscopic ligation of acute esophageal variceal bleeding in patients with liver cirrhosis. Acta Gastroenterol Belg. 2020;83.
274. Ibrahim E, Abdel-Samiee M, Youssef MI, El-Shazly H, A. El-Gendy A, Sakr AA, et al. Variceal recurrence 4 years post endoscopic band ligation in hepatitis C patients who achieved sustained virological response with oral direct-acting antiviral therapy. J Viral Hepat. 2021;28(2):279–87.
275. Mohammed SEA, Abdo AE, Mudawi HMY. Mortality and rebleeding following variceal haemorrhage in liver cirrhosis and periportal fibrosis. World J Hepatol. 2016;8(31):1336.
276. Kamaoui I, Maaroufi M, Oussaden A, Abid H, Boubou M, Houssaini NS, et al. Small bowel varices: value of abdominal CT angiography. J Radiol. 2011;92(10):933–5.
277. Gad YZ, Zeid AA. Portal hypertensive colopathy and haematochezia in cirrhotic patients: an endoscopic study. Arab J Gastroenterol. 2011;12(4):184–8.
278. Serag WM, eldeen Mohammed BS, Mohamed MM, Elsayed BE. Predicting the risk of portal vein thrombosis in patients with liver cirrhosis and hepatocellular carcinoma. Heliyon. 2020;6(8):e04677.
279. Abdel-Razik A, Mousa N, Elhelaly R, Tawfik A. De-novo portal vein thrombosis in liver cirrhosis: risk factors and correlation with the Model for End-stage Liver Disease scoring system. Eur J Gastroenterol Hepatol. 2015;27(5):585–92.
280. Gabr MA, Bessa SSE, El-Zamarani EA. Portal vein thrombosis in Egyptian patients with liver cirrhosis: Role of methylenetetrahydrofolate reductase C677T gene mutation. Hepatol Res. 2010;40(5):486–93.
281. Khayyat YM. Survival of patients with portal vein thrombosis: analysis based on disease onset. Hepatogastroenterology. 2013;60(121):65–9.
282. Ghobrial C, Rabea M, Mohsen N, Eskander A. Gastric antral vascular ectasia in portal hypertensive children:

endoscopic band ligation versus argon plasma coagulation. J Pediatr Surg. 2019;54(8):1691–5.
283. El-Sayed R, Abou El-Ela M, El-Raziky MS, Helmy H, Abd El-Ghaffar A, El-Karaksy H. Relation of serum levels of thrombopoietin to thrombocytopenia in extrahepatic portal vein obstruction versus cirrhotic children. J Pediatr Hematol Oncol. 2011;33(7):e267–70.
284. Helaly AZ, Al-Warraky MS, El-Azab GI, Kohla MAS, Abdelaal EE. Portal and splanchnic hemodynamics after partial splenic embolization in cirrhotic patients with hypersplenism. Apmis. 2015;123(12):1032–9.
285. Desouky M. VEGF and PDGF in liver cirrhosis and their relation to echocardiographic parameters and Carotid Intima-Media Thickness. Life Sci J. 2013;10(4).
286. Barakat AAE-K, Nasr FM, Metwaly AA, El-Ghannam M. Systemic vascular resistance and fluid status in patients with decompensated liver cirrhosis with or without functional renal failure in Egypt. Electron Physician. 2015;7(4):1174.
287. Mustafa Y, Saleh A, Elassal G, Elsayed A. Assessment of pulmonary hypertension in patients with liver disease pre and post liver transplantation. Egypt J Chest Dis Tuberc. 2014;63(1):213–8.
288. Osman MA, Sayed MM, Mansour KA, Saleh SA, Ibrahim WA, Abdelhakam SM, et al. Reversibility of minimal hepatic encephalopathy following liver transplantation in Egyptian cirrhotic patients. World J Hepatol. 2016;8(30):1279.
289. Kobtan AA, El-Kalla FS, Soliman HH, Zakaria SS, Goda MA. Higher grades and repeated recurrence of hepatic encephalopathy may be related to high serum manganese levels. Biol Trace Elem Res. 2016;169(2):153–8.
290. Yadav SK, Goel A, Saraswat VA, Thomas MA, Wang E, Marincola FM, et al. Evaluation of cognitivity, proinflammatory cytokines, and brain magnetic resonance imaging in minimal hepatic encephalopathy induced by cirrhosis and extrahepatic portal vein obstruction. J Gastroenterol Hepatol. 2016;31(12):1986–94.
291. Amer ME, ABDEL KHALIK MAR, Khedr MAHB, Massoud SAMA. Effect of helicobacter pylori eradicationon the pathogenesis of minimal hepatic encephalopathy in egyptian patients with liver cirrhosis. J Egypt Soc Parasitol. 2018;48(3):583–6.
292. Esmat S, El Garem N, Raslan H, Elfekki M, Sleem GA. Critical flicker frequency is diagnostic of minimal hepatic encephalopathy. J Investig Med. 2017;65(8):1131–5.
293. Abdelrahman ME, Mahmoud SZ, Ali AM, El-Khateeb HAAT, Mohamed GA. Screening for minimal hepatic encephalopathy among asymptomatic drivers with chronic liver disease. Egypt J Intern Med. 2018;30(4):217–22.
294. Razek AAKA, Abdalla A, Ezzat A, Megahed A, Barakat T. Minimal hepatic encephalopathy in children with liver cirrhosis: diffusion-weighted MR imaging and proton MR spectroscopy of the brain. Neuroradiology. 2014;56(10):885–91.
295. Ashour S, Gaber A, Aly OA, Hashem S, Salama MM, Shalash AS. A Study of Extrapyramidal Manifestations Accompanying Decompensated Viral Hepatic Cirrhosis Patients. Rev Recent Clin Trials. 2017;12(3):162–7.
296. Tharwa E-S, Mohamed A, Elshazly H, Salama M, Youssef MI, Bakeer MS, et al. Sudomotor changes in hepatitis C virus infection with or without diabetes mellitus: a pilot study in Egyptian patients. Am J Trop Med Hyg. 2021;104(2):580.
297. Shaat MM, Hamza SA, Mahmoud NH, Ali SM, Abou-Hashem RM. The Relationship between Trace Elements and Depression among Older Patients with Chronic Liver Disease. Electron J Gen Med. 2020;17(5).
298. Helal EM, Sharaf-Eldin M, Abou El Azm AR, Badr Eldin NM, Dawoud MM, Abd-Elsalam S, et al. Hemodynamic changes of hepatic & renal vessels in systemic bacterial infection with fever in HCV related cirrhosis. Infect Disord Targets (Formerly Curr Drug Targets-Infectious Disord. 2020;20(4):511–6.
299. Metwally K, Fouad T, Assem M, Abdelsameea E, Yousery M. Predictors of spontaneous bacterial peritonitis in patients with cirrhotic ascites. J Clin Transl Hepatol. 2018;6(4):372.
300. Elfert A, Abo Ali L, Soliman S, Ibrahim S, Abd-Elsalam S. Randomized-controlled trial of rifaximin versus norfloxacin for secondary prophylaxis of spontaneous bacterial peritonitis. Eur J Gastroenterol Hepatol. 2016;28(12):1450–4.
301. Abdel-Razik A, Mousa N, Elbaz S, Eissa M, Elhelaly R, Eldars W. Diagnostic utility of interferon gamma-induced protein 10 kDa in spontaneous bacterial peritonitis: single-center study. Eur J Gastroenterol Hepatol. 2015;27(9):1087–93.
302. Salman TA, Edrees AM, El-Said HH, El-Abd OL, El-Azab GI. Effect of different therapeutic modalities on systemic, renal, and hepatic hemodynamics and short-term outcomes in cirrhotic patients with spontaneous bacterial peritonitis. Eur J Gastroenterol Hepatol. 2016;28(7):777–85.
303. Abdel-Razik A, Mousa N, Elhammady D, Elhelaly R, Elzehery R, Elbaz S, et al. Ascitic fluid calprotectin and serum procalcitonin as accurate diagnostic markers for spontaneous bacterial peritonitis. Gut Liver. 2016;10(4):624.
304. El-Shabrawi MHF, El-Sisi O, Okasha S, Isa M, Elmakarem SA, Eyada I, et al. Diagnosis of spontaneous bacterial peritonitis in infants and children with chronic liver disease: A cohort study. Ital J Pediatr. 2011;37(1):1–7.
305. Sabobeh T, Mushtaq K, Elsotouhy A, Ammar AA, Rashid S. Invasive rhinocerebral mucormycosis in a patient

with liver cirrhosis leading to fatal massive stroke. Med Mycol Case Rep. 2018;22:69–73.
306. Arabi YM, Dara SI, Memish Z, Al Abdulkareem A, Tamim HM, Al-Shirawi N, et al. Antimicrobial therapeutic determinants of outcomes from septic shock among patients with cirrhosis. Hepatology. 2012;56(6):2305–15.
307. Hassan EA, Abd El-Rehim AS, Hassany SM, Ahmed AO, Elsherbiny NM, Mohammed MH. Fungal infection in patients with end-stage liver disease: low frequency or low index of suspicion. Int J Infect Dis. 2014;23:69–74.
308. Mohammed BJ. Association between TNF-alpha level and TNF-alpha gene polymorphisms in liver cirrhosis of Iraqi patients. Biosci Res. 2018;15(2):1342–9.
309. Talaat RM, Noweir YM, Elmaghraby AM, Elsabaawy MM, Mohamed E-S. TNF-related apoptosis-inducing ligand (TRAIL), death receptor (DR4) and Fas gene polymorphisms associated with liver cirrhosis in hepatitis C infected patients. Gene Reports. 2021;22:101018.
310. Bizid S, Yacoub H, Mohamed G, Ben Slimane B, Boughoula K, Ben Abdallah H, et al. Does Anemia Have a Potential Effect on Type 2 Hepatorenal Syndrome? Can J Gastroenterol Hepatol. 2020;2020.
311. Abdel-Razik A, Mousa N, Abdelsalam M, Abdelwahab A, Tawfik M, Tawfik AM, et al. Endothelin-1/nitric oxide ratio as a predictive factor of response to therapy with terlipressin and albumin in patients with type-1 hepatorenal syndrome. Front Pharmacol. 2020;11:9.
312. Soliman AR, Ahmed RM, Abdalla A, Soliman M, Saeed M. Impact of Enterobacteriaceae bacteremia on survival in patients with hepatorenal failure. Saudi J Kidney Dis Transplant. 2018;29(6):1311.
313. Watany MM, Hagag RY, Okda HI. Circulating miR-21, miR-210 and miR-146a as potential biomarkers to differentiate acute tubular necrosis from hepatorenal syndrome in patients with liver cirrhosis: a pilot study. Clin Chem Lab Med. 2018;56(5):739–47.
314. Elfaramawy AAM. Hepatoadrenal syndrome in Egyptian children with liver cirrhosis with and without sepsis. Egypt J Med Hum Genet. 2012;13(3):337–42.
315. Alghamdi SA, Saadah OI, Almatury N, Al-Maghrabi J. Hepatic-associated immunoglobulin-A nephropathy in a child with liver cirrhosis and portal hypertension. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2012;18(3):214.
316. Aljumah AA, Tamim H, Saeed M, Tamimi W, Alfawaz H, Al Qurashi S, et al. The role of urinary neutrophil gelatinase-associated lipocalin in predicting acute kidney dysfunction in patients with liver cirrhosis. J Clin Med Res. 2018;10(5):419.
317. Omar M, Abdel-Razek W, Abo-Raia G, Assem M, El-Azab G. Evaluation of serum cystatin C as a marker of early renal impairment in patients with liver cirrhosis. Int J Hepatol. 2015;2015.
318. Alhaddad OM, Alsebaey A, Amer MO, El-Said HH, Salman TAH. Neutrophil gelatinase-associated lipocalin: a new marker of renal function in C-related end stage liver disease. Gastroenterol Res Pract. 2015;2015.
319. Qasem AA, Farag SE, Hamed E, Emara M, Bihery A, Pasha H. Urinary biomarkers of acute kidney injury in patients with liver cirrhosis. Int Sch Res Not. 2014;2014.
320. Hessien M, Ayad M, Ibrahim WM, Ularab BI. Monitoring coagulation proteins during progression of liver disease. Indian J Clin Biochem. 2015;30(2):210–6.
321. Baccouche H, Labidi A, Fekih M, Mahjoub S, Kaabi H, Hmida S, et al. Haemostatic balance in cirrhosis. Blood Coagul Fibrinolysis. 2017;28(2):139–44.
322. Mohamed SE, Yassin MA. Eltrombopag Use for Treatment of Thrombocytopenia in a Patient with Chronic Liver Disease and Portal Vein Thrombosis: Case Report. Case Rep Oncol. 2020;13(2):863–6.
323. Fouad R, Hamza I, Khairy M, Elsharkawy M, Helmy AA. Role of serum soluble CD163 in the diagnosis, risk of bleeding, and prognosis of gastro-esophageal varices in cirrhotic patients. J Interf Cytokine Res. 2017;37(3):112–8.
324. El-Sayed R, El-Karaksy H, El-Raziky M, El-Hawary M, El Koofy N, Helmy H, et al. Assessment of coagulation and fibrinolysis in children with chronic liver disease. Blood Coagul Fibrinolysis. 2013;24(2):113–7.
325. Hammami R, Boudabbous M, Jdidi J, Trabelsi F, Mroua F, Kallel R, et al. Cirrhotic cardiomyopathy: is there any correlation between the stage of cardiac impairment and the severity of liver disease? Libyan J Med. 2017;12(1).
326. Héla E, Sofien K, Kamel L, Asma O, Dalila G, Sondos K, et al. QT interval abnormalities and heart rate variability in patients with cirrhosis. Arab J Gastroenterol. 2020;21(4):246–52.
327. Omran DA, Behairy NHELD, Zakaria KS, Nabil MM, Said K. Functional and morphological myocardial changes in hepatitis C virus patients with end-stage liver disease. Scand J Gastroenterol. 2015;50(9):1135–43.
328. Ali AA, Abdel-Atty HE, Azab NY, El-Wahsh RA, Dawood AE-DE, El-Gazzar HM. Cardiopulmonary exercise testing in patients with liver cirrhosis. Egypt J Chest Dis Tuberc. 2015;64(4):959–62.
329. Sharaf-Eldin M, Bediwy AS, Kobtan A, Abd-Elsalam S, El-Kalla F, Mansour L, et al. Pigtail catheter: a less invasive option for pleural drainage in Egyptian patients with recurrent hepatic hydrothorax. Gastroenterol Res Pract. 2016;2016.
330. Mahmoud E, Anwar M. Comparison of tigecycline and bleomycin pleurodesis by pigtail catheter in hepatic hydrothorax with liver cirrhosis. Egypt J Chest Dis Tuberc. 2020;69(1):98.
331. Rezk NA, El-Maleky NA. Pulmonary function changes after ethanolamine oleate injection VS band ligation in the treatment of esophageal varices. Egypt J Chest Dis Tuberc. 2013;62(4):769–73.

332. Abdel-bary SA, Yousif M, Hussein HA. Respiratory muscle strength, hypoxemia and dyspnea in liver cirrhosis patients. Egypt J Chest Dis Tuberc. 2014;63(4):1059–64.
333. Helmy AM, Awadallah MF. Study of pulmonary dysfunctions in liver cirrhosis. Egypt J Chest Dis Tuberc. 2014;63(4):1079–85.
334. AE MAAEM, Elakad A, Ali A, Abd-Elkader M, Sayed AF, Taha A, et al. Hepatopulmonary syndrome: prevalence and predictors in Egyptian cirrhotic patients. Trop Gastroenterol. 2011;32(1):25–30.
335. Muhsen IN, AlFreihi O, Abaalkhail F, AlKhenizan A, Khan M, Eldali A, et al. Bone mineral density loss in patients with cirrhosis. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2018;24(6):342.
336. Almulaify MS, Alwadei FAA, Aljaroudi RA, Alomran ST. THE PREVALENCE OF OSTEOPOROSIS IN PATIENTS WITH LIVER CIRRHOSIS. INDO Am J Pharm Sci. 2018;5(11):11292–7.
337. Al-Mendalawi M. Bone mineral density loss in patients with cirrhosis. Saudi J Gastroenterol. 2019;25(3):201.
338. Mohamed SY, Emara MH, Gabballah BA, Mostafa EF, Maaly MA. Effects of Ramadan fasting on Muslim patients with liver cirrhosis: A comparative study. Govaresh. 2018;23(1):47–52.
339. Mohamed SY, Emara MH, Hussien HIM, Elsadek HM. Changes in portal blood flow and liver functions in cirrhotics during Ramadan fasting in the summer; a pilot study. Gastroenterol Hepatol from Bed to Bench. 2016;9(3):180.
340. Elkholy S, Mogawer S, Sherif H, Mansour M, Mogawer E. SIGNIFICANCE OF NUTRITION ASSESSMENT AND NUTRITION SCREENING TOOLS IN PREDICTING COMPLICATIONS AMONG PATIENTS WITH LIVER CIRRHOSIS. In: TRANSPLANT INTERNATIONAL. WILEY-BLACKWELL 111 RIVER ST, HOBOKEN 07030-5774, NJ USA; 2013. p. 87.
341. Elkabbany ZA, Hamza RT, Mahmoud NH. Assessment of serum acylated ghrelin in children and adolescents with chronic liver diseases: relation to nutritional status. Sci World J. 2014;2014.
342. Mabrouk AA, Nooh MA, Azab NY, Elmahallawy II, Elshenawy RHM. Sleep pattern changes in patients with liver cirrhosis. Egypt J Chest Dis Tuberc. 2012;61(4):447–51.
343. Fares A-J, Ahmed AE, Shirbini N, Abdullah A-H, Salim B, Ali YZ, et al. Symptoms of daytime sleepiness and sleep apnea in liver cirrhosis patients. Ann Hepatol. 2017;16(4):591–8.
344. Hanafy AS, Hassaneen AM. Rifaximin and midodrine improve clinical outcome in refractory ascites including renal function, weight loss, and short-term survival. Eur J Gastroenterol Hepatol. 2016;28(12):1455–61.
345. Ali A, Farid S, Amin M, Kassem M, Al-Garem N, Al-Ghobashy M. Comparative Clinical Pharmacokinetics of Midodrine and Its Active Metabolite Desglymidodrine in Cirrhotic Patients with Tense Ascites Versus Healthy Volunteers. Clin Drug Investig. 2016;36(2):147–55.
346. Salama H, Zekri A-RN, Ahmed R, Medhat I, Abdallah ES, Darwish T, et al. Assessment of health-related quality of life in patients receiving stem cell therapy for end-stage liver disease: an Egyptian study. Stem Cell Res Ther. 2012;3(6):1–10.
347. Salama H, Zekri A-RN, Medhat E, Al Alim SA, Ahmed OS, Bahnassy AA, et al. Peripheral vein infusion of autologous mesenchymal stem cells in Egyptian HCV-positive patients with end-stage liver disease. Stem Cell Res Ther. 2014;5(3):1–12.
348. Amin MA, Sabry D, Rashed LA, Aref WM, el-Ghobary MA, Farhan MS, et al. Short-term evaluation of autologous transplantation of bone marrow–derived mesenchymal stem cells in patients with cirrhosis: Egyptian study. Clin Transplant. 2013;27(4):607–12.
349. Hofny ERM, Ali MEM, Taha EA, Nafeh HM, Sayed DS, Abdel-Azeem HG, et al. Semen and hormonal parameters in men with chronic hepatitis C infection. Fertil Steril. 2011;95(8):2557–9.
350. Ezzikouri S, El Feydi AE, Afifi R, Benazzouz M, Hassar M, Pineau P, et al. Impact of TP53 Codon 72 and MDM2 Promoter 309 Allelic Dosage in a Moroccan Population with Hepatocellular Carcinoma. Int J Biol Markers [Internet]. 2011 Jul 1;26(4):229–33. Available from: https://doi.org/10.5301/JBM.2011.8881
351. Akil A, Ezzikouri S, El Feydi AE, Benazzouz M, Afifi R, Diagne AG, et al. Associations of genetic variants in the transcriptional coactivators EP300 and PCAF with hepatocellular carcinoma. Cancer Epidemiol [Internet]. 2012;36(5):e300–5. Available from: https://www.sciencedirect.com/science/article/pii/S1877782112000720
352. Foliaki S, Brewer N, Pearce N, Snijders PJF, Meijer CJLM, Waqatakirewa L, et al. Prevalence of HPV infection and other risk factors in a Fijian population. Infect Agent Cancer [Internet]. 2014;9(1):14. Available from: https://doi.org/10.1186/1750-9378-9-14
353. Ezzikouri S, Alaoui R, Tazi S, Nadir S, Elmdaghri N, Pineau P, et al. The adiponutrin I148M variant is a risk factor for HCV-associated liver cancer in North-African patients. Infect Genet Evol [Internet]. 2014;21:179–83. Available from: https://www.sciencedirect.com/science/article/pii/S1567134813004176
354. Jadid FZ, Chihab H, Alj HS, Elfihry R, Zaidane I, Tazi S, et al. Control of progression towards liver fibrosis and hepatocellular carcinoma by SOCS3 polymorphisms in chronic HCV-infected patients. Infect Genet Evol [Internet]. 2018;66:1–8. Available from: https://www.sciencedirect.com/science/article/pii/S1567134818303186

355. Rahamtalla FA, Abdalla MSM, Mudawi SBM, Kheir Elsid MAH, Shammat IM. Estimation of telomerase, AFP, and AFP-L3 levels in Sudanese patients with hepatocellular carcinoma and chronic liver diseases. Comp Clin Path [Internet]. 2018;27(5):1133–40. Available from: https://doi.org/10.1007/s00580-018-2709-2
356. Al-sarayreh S, Al-shuneigat J, Al-saraireh YM. Evaluating some biomarkers for diagnosis , Hepatocellular Carcinoma patients from Jordan. 2020;(February).
357. Farag RMA, Al Ayobi D, Alsaleh KA, Kwon H-J, EL-Ansary A, Dawoud EA. Studying the Impact of Golgi Protein 73 Serving as a Candidate Biomarker in Early Diagnosis for Hepatocellular Carcinoma among Saudi Patients. Asian Pac J Cancer Prev. 2019 Jan;20(1):215–20.
358. Al-Zoubi S, Wassouf A, Zetoune AB. Measuring levels of osteopontin as potential biomarker for hepatocellular carcinoma in Syrian patients. Gastroenterol Hepatol from bed to bench. 2017;10(2):97–101.
359. Dhifallah I, Khedhiri M, Chouikha A, Kharroubi G, Hammami W, Sadraoui A, et al. Hepatitis viruses take advantage of traditional practices to increase the burden of hepatocellular carcinoma in Tunisia. Arch Virol [Internet]. 2020;165(1):33–42. Available from: https://doi.org/10.1007/s00705-019-04440-5
360. Bahri O, Ezzikouri S, Alaya-Bouafif N Ben, Iguer F, Feydi AE El, Mestiri H, et al. First multicenter study for risk factors for hepatocellular carcinoma development in North Africa. World J Hepatol. 2011 Jan;3(1):24–30.
361. Shaker MK, Abdella HM, Khalifa MO, Dorry AK El. Epidemiological characteristics of hepatocellular carcinoma in Egypt: a retrospective analysis of 1313 cases. Liver Int [Internet]. 2013 Nov 1;33(10):1601–6. Available from: https://doi.org/10.1111/liv.12209
362. Abd-elsalam S, Elwan N, Soliman H, Ziada D, Elkhalawany W, Salama M, et al. Gastro-intestinal & Hepatobiliary Cancer Epidemiology of liver cancer in Nile delta over a decade : A single - center study. 2020;24–6.
363. Rasul KI, Al-Azawi SH, Chandra P. Hepatocellular carcinoma in qatar. Gulf J Oncol. 2013;1(14):70–5.
364. Qari YA, Mosli MH. Epidemiology and clinical features of patients with hepatocellular carcinoma at a tertiary hospital in Jeddah. 2017;43–7.
365. Alghamdi IG, Alghamdi MS. The Incidence Rate of Liver Cancer in Saudi Arabia: An Observational Descriptive Epidemiological Analysis of Data from the Saudi Cancer Registry (2004-2014). Cancer Manag Res. 2020;12:1101–11.
366. Ziada DH, El Sadany S, Soliman H, Abd-Elsalam S, Salama M, Hawash N, et al. Prevalence of hepatocellular carcinoma in chronic hepatitis C patients in Mid Delta, Egypt: A single center study. J Egypt Natl Canc Inst [Internet]. 2016;28(4):257–62. Available from: https://www.sciencedirect.com/science/article/pii/S1110036216300322
367. Samia, M. Sanad, Amal, M. Mangoud AAS and MSAE-W. Histopathological and Immunohistochemical Studies on the Liver of Chronic Hepatitis C Virus Infected Patients and Hepatocellular Carcinoma in Sharkia Governorate, Egypt Samia,. 2011;8(4):1008–25.
368. Ferroudj S, Yildiz G, Bouras M, Iscan E, Ekin U, Ozturk M. Role of Fanconi anemia/BRCA pathway genes in hepatocellular carcinoma chemoresistance. Hepatol Res [Internet]. 2016 Nov 1;46(12):1264–74. Available from: https://doi.org/10.1111/hepr.12675
369. Alswat KA, Sanai FM, Altuwaijri M, Albenmousa A, Almadi M, Al-hamoudi WK, et al. Clinical Characteristics of Patients with Hepatocellular Carcinoma in a Mid- dle Eastern Population. 2013;13(5):1–8.
370. Al-Naamani K, Al-Hashami Z, Al-Siyabi O, Al-Moundri M, Al-Bahrani B, Al-Sinani S, et al. Hepatocellular Carcinoma in Oman: An analysis of 284 cases. Sultan Qaboos Univ Med J. 2020 Aug;20(3):e316–22.
371. Limaiem Faten, Bouhamed Marwa, Sahraoui Ghada MS. Hepatocellular carcinoma: a clinicopathological study of 64 cases. 2017;8688.
372. Helal TEA, Radwan NA, Shaker M. Extrahepatic metastases as initial manifestations of hepatocellular carcinoma: an Egyptian experience. Diagn Pathol [Internet]. 2015;10(1):82. Available from: https://doi.org/10.1186/s13000-015-0313-1
373. Elian MMM, Gawad EAA. The many, atypical presentations of musculoskeletal hepatocellular carcinoma (HCC) metastases. Egypt J Radiol Nucl Med [Internet]. 2014;45(4):1183–92. Available from: https://www.sciencedirect.com/science/article/pii/S0378603X14001624
374. Al-Muhannadi N, Ansari N, Brahmi U, Satir AA. Differential diagnosis of malignant epithelial tumours in the liver: An immunohistochemical study on liver biopsy material. Ann Hepatol. 2011;10(4):508–15.
375. Marsico M, Gabbani T, Lunardi S, Galli A, Biagini MR, Annese V. Percutaneous ultrasound-guided fiducial marker placement for liver cancer robotic stereotactic radio-surgery treatment: A comparative analysis of three types of markers and needles. Arab J Gastroenterol [Internet]. 2017;18(2):83–6. Available from: https://www.sciencedirect.com/science/article/pii/S1687197917300370
376. McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of Hepatocellular Carcinoma. Hepatology [Internet]. 2021 Jan1;73(S1):4–13. Available from: https://doi.org/10.1002/hep.31288
377. Siegel RL, Torre LA, Soerjomataram I, Hayes RB, Bray F, Weber TK, et al. Global patterns and trends in colorectal cancer incidence in young adults. Gut [Internet]. 2019 Dec

1;68(12):2179 LP – 2185. Available from: http://gut.bmj.com/content/68/12/2179.abstract