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LIVER DISEASE IN AFRICA 2019

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INTRODUCTION

The 2nd Conference on Liver Disease in Africa (COLDA 2019) was held in Cairo Egypt. During the 2nd edition, a platform was created that provided a unique opportunity for clinicians, researchers, policy makers, industry and other healthcare professionals in the African region to come together and exchange knowledge on the lasts clinical developments and updates on ongoing and new trials related to liver disease.

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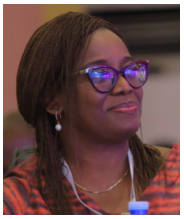

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Globally 257 million people are infected with Hepatitis B virus (HBV) of which approximate 60 million are living in the African region and 21 million in the Eastern-Mediterranean region. Additionally, worldwide 71 million people are infected with Hepatitis C virus (HCV), from which 11 million are in the African region and 15 million in the Eastern-Mediterranean region. This resulting in the total burden of viral hepatitis being higher as compared to HIV, tuberculosis (TB) and malaria combined[1,2].

With the availability of highly effective antivirals the elimination of viral hepatitis became feasible on a biological and technical level. Therefore, the World Health Assembly unanimously adopted a resolution proposing the elimination of viral hepatitis by 2030. In addition, the WHO published the Global Health Sector Strategy on viral hepatitis with cornerstones to reach this goal[1]. The declaration to eliminate viral hepatitis as a public health threat not only led to elimination plans but was also a call to action and the need for health equity[3]. Regardless of the many successes obtained in the past years many challenges remain before the elimination of viral hepatitis is achieved. Especially on the African continent where for example the high number of undiagnosed patients and limited infrastructure and resources remains a key problem[4].

Egypt is leading in the progress towards HCV elimination and therefore a great example of a successful national HCV program in a country with limited resources. Previously, Egypt had the highest global HCV prevalence. The Egyptian government has therefore declared that HCV as a major public health issue as soon as antiviral therapy became available. With major presidential support and government funding an HCV elimination program was started. Low-cost generics were combined with low cost diagnostic tools, due to prosperously negotiations regarding mass-purchasing prices for diagnostics. This all resulted in a rapid scale-up of direct-acting antiviral (DAA) therapy[5]. While Egypt was very successful in treating all known HCV cases, many individuals remained undiagnosed. and massive testing programmes were needed to identify the missing millions[6]. Successful screenings programs were established, which not only included screening for HCV and HBV, but also for obesities, diabetes, and hypertension. By further simplifying diagnostics, the cost per eliminated HCV case declined.

Egypt was not the only country with a successful national HCV elimination plan. The government in Rwanda, also acknowledged viral hepatitis as a major health problem and sought funding for a national elimination plan. For many years now, HCV is systematically screened in donated blood and training for safe injection practices among health-care workers are provided. Since 2011, the national hepatitis control unit is active, and the first viral hepatitis guidelines were developed and disseminated. In Rwanda HCV diagnostics is integrated within HIV testing systems resulting in lower screening costs. DAA therapy is available at $80 per treatment course and can be prescribed by 110 physicians from district hospitals. Currently, partnerships are being developed and nurses are trained in HCV care and treatment[7].

Civil society can be very useful to eliminate viral hepatitis as they provide more insights into the needs of the community, reach the underserved population, and understand stigma and discrimination. Moreover, they can create advocacy and awareness, needed to push viral hepatitis elimination on the political agenda. Patient groups can help to test-and-treat, vaccinate or link diagnosed people to care. Community led educate, test-and-treat demonstration projects were successful in achieving a high uptake of HCV testing, treatment, and linkage to care in rural Africa. Additionally, cure rates as well as awareness and adoption of prevention strategies were high in the community showing that community led approached are important elimination strategies in rural settings[8,9].

HEPATITIS B VIRUS (HBV)

HBV elimination is moving slow as diagnosis rates are low ranging from <1% in sub-Saharan Africa (SSA) to 42% in European countries. Unfortunately, this is nowhere close to the WHO elimination goals. The presence of a cure would highly improve these numbers and accelerate the reduction of HBV incidence, decrease the risk of hepatocellular carcinomas (HCC), and rapidly reduce costs of reaching the elimination targets. Nevertheless, the missing millions should be identified, and a cure needs to be present, which is a matter of time. Currently, treatment for HBV is available but should be taken lifelong as HBsAG seroconversion is rare. It is unclear if HBV therapy is suitable for Africa due to higher retention rates compared to Europe and the US. Overall therapy adherence in Africa is low, patients often experience side-effects, and many do not experience HBV symptoms. Adequate therapy would be beneficial as it reduces the numbers of cirrhosis, HCC, and provides seroconversion to anti-HBeAG in 1/3 of patients.

The complex HBV algorithm does not contribute towards good HBV care and simplification is needed. Recommended is that only patients in the immune clearance and reactivation phase (HBsAG+, fluctuating ALT levels, HBV-DNA+, changes in liver biopsies, and HBeAG-/+) should receive therapy. Additionally, patients with extra hepatic manifestations, compensated and decompensated cirrhosis, or patients with a family history of HCC or cirrhosis are also eligible. The first-line therapy for naïve patients includes Entecavir or Tenofovir. If patients are on Lamivudine this can be continued with regular monitoring. When Lamivudine is combined with Adefovir this can be continued or a switch to Tenofovir can be made since this is less costly. HBV can be reactivated through DAA therapy therefore HBV and prophylaxis until week 12 post DAAs is needed in HBsAG + patients. HBsAG- antiHBc+ patients should be monthly monitored by measuring ALT-levels. Patients who are no eligible for therapy should receive six monthly monitoring and liver fibrosis assessments every 2 years. Non-invasive methods assessing the severity of the liver disease are scoring the APRI and FIB.

Ethiopia is one of the African countries which set solid HBV elimination plans by adopting a national guideline. Furthermore, health care workers are trained on a national level, health care providers are vaccinated, and awareness is created. Moreover, HBV care is decentralized and integrated in HIV care following a similar diagnostic platform. Several challenges occurred as patients have a lack towards presenting for care and data is unorganized into a solid system. Moreover, screening and viral load testing remain an issue and liver biopsies cannot be decentralized. Fibro-scans are costly, and non-invasive fibrosis markers for chronic HBV are not assessed on reliability in Africa[10]. For example, a poor diagnostic accuracy compared to liver biopsy was found for the APRI in a cohort of West African patients with chronic HBV (sensitivity 0-9%). Moreover, the WHO guidelines did not detect half of patients in need for treatment in Ethiopia[11]. Most patients (52%) who fulfilled the WHO criteria already had decompensated cirrhosis suggesting that the opportunity to treat and protect enough patients with chronic HBV from decompensation and liver cancer is overlooked.

Several SSA countries have a high HCV burden; Nigeria, DR Congo, Ethiopia, Angola, Ghana[5]. Moreover, new HCV infections occur due to unsafe injections, blood transfusions, and through traditional practices. Among PWIDs the HCV prevalence is estimated at 30-50% and prevalence among MSM is unknown as quantification of the MSM population is impossible. The SSA region still lacks behind on the numbers of patients who are treated (<3%), although responses are increasing. Currently, 67% of African countries have viral hepatitis focal points but only one-third have technical teams in place. Additionally, only 20% of countries have published national hepatitis plans and the awareness and political will towards viral hepatitis in general should be increased on the African continent. There is clear evidence that investment in HCV elimination returns in major benefits in terms of lower morbidity and mortality[7,12-14]. Therefore, the investment case should be well presented towards policy makers.

Limited data on the success rates of DAA therapy in SSA are available but those who are were promising[15]. Nevertheless, DAA therapy is more challenging due to the large diversity of HCV in SSA. Especially among the unusual subtypes (GT1 non 1a/b and GT4 non 4a/d) DAA failure occurs more frequently[16]. These substantial number of failure are driven by the occurrence of polymorphisms at baseline compared to the most sensitive subtype[15,17]. In SSA, retreatment of DAA failures is even more difficult since the approved regimens (sofosbuvir+velpatasvir+voxilaprevir and glecaprevir+pibrentasvir) have limited experience among these unusual subtypes and more importantly are unavailable in the region.

HEPATITIS DELTA VIRUS (HDV)

Hepatitis delta virus (HDV) is a virus, with eight different genotypes and several sub-genotypes, dependent on the presence of the HBV. Therefore, only HBsAG+ patients can be infected with HDV. HDV can occur as a coinfection were both infections incurred at the same time point. However, HBV must be established first during the acute co-infection before HDV can spread. The combination of HBV/HDV results in more severe cases as compared to HBV mono-infections alone[18].

HBsAG+ patients can also be infected with HDV, also called a super infection. A superinfection presents as a severe acute hepatitis or flare-up of chronic HBV. The clinical course is more severe than an HBV/HDV co-infection since the presence of HBsAG allows for continuously replication. Therefore, these patients often progress towards a chronic HDV infection. Again the presence of HDV results in more complications and a higher morbidity than an HBV-mono infection[19].

HDV prevalence can only be measured among HBsAG carriers. More specifically, among HBsAG carriers with advanced liver disease as HDV is more pathogenic than HBV (70% of cases progress towards cirrhosis within 5-10 years). Currently, many countries report a zero-low HDV prevalence which is measured among "healthy" populations, e.i. blood donors, and therefore often an underestimation. HDV prevalence reports among the HBsAG population in Africa mention a prevalence of 5.1% (7 million individuals) in North Africa and 8,39% (7 million individuals) in Sub-Saharan Africa20,21. PEG-INFα is the only effective drug against HDV.

HDV is an important cause of liver disease but data are limited, sparse, and heterogeneous. There is an urgent need for systematically collected data, particularly for east and south Africa. Moreover, genotypes 5-8 are unique to Africa and clinical characterization is needed.

Viral hepatitis during pregnancy is a fast topic which needs more addressing. New viral hepatitis infections still occur with major consequences for both mother and foetus. An annual estimated number of 360,000 infants are perinatal infected with HBV (190,000 with HIV)22. Preventing perinatal HBV infection is key as early acquired HBV infections result in a 90% risk of chronicity. Moreover, the risk of obtaining HCC is higher[23].

Antenatal HBsAG screening should be performed in the first trimester followed by HBeAG and when positive by HBV DNA. HBeAG positivity varies from 10-30% over several African regions. HBV vaccination should be provided to women with no immune response and is safe during pregnancy. Unfortunately, for most HBV infected pregnant women HBV treatment is unsuitable, which increases the change by pre-labour transmission. HBV can be treated with tenofovir, which has an excellent safety record in pregnancy among HIV infected woman with no increase in birth defects compared to the general population (i.e. 2%)[24].

The birth-dose can easily overcome the problem of pre- and post-labour transmission. Currently, on the African continent, only 70% of countries have implemented birth dose vaccinations in an EPI schedule at week 6,10, and 14, despite the evidence of cost-effectiveness. Administration of the birth dose within 24 hours after birth is highly recommended although a challenge due to the many homebirths. The HBV birth dose is supported by GAVI in GAVI eligible countries to increase the vaccination coverage.

For women at risk for HCV infection, anti-HCV should be screened during the first prenatal visit and repeated during pregnancy. If exposure to HCV happened in the last six months and the ani-HCV test is negative, an HCV-PCR test should be performed. It is unknown if acute HCV increases the risk of mother-to-child-transmission (MTCT) or is associated with more adverse pregnancy outcomes. Chronic HCV does result in a greater risk of infertility, a higher rate of gestational diabetes, and less live births. HCV MTCT is not affected by breast-feeding, however when nipples are cracked and bleeding abstention is required[25]. Infants who were born to HCV-infected mothers should be screened with an HCV-PCR when >1 month of age or by an anti-HCV when >18 months of age. HCV can be treated with sofosbuvir/ledipasvir in children over 3 – 12 years of age for genotype 1,4,5, and 6[26].

The Hepatitis E virus (HEV) is the viral hepatitis with the most severe consequences for both mother and child. HEV infections result in a 26% maternal and 33% foetal mortality. Moreover, in 45% of cases a fulminant hepatic failure occurred, associated with the highest case rate fatality. HEV is also related to preterm labour, premature rupture of membranes, postpartum haemorrhage, and a low birth weight.

The pooled HEV IgG seroprevalence among pregnant women in Africa was estimated around 29% with the highest prevalence in Egypt (84%) and lowest in Gabon (7%)[27]. Vertical transmission ranged from 28-79%. Currently, no commercial vaccination is available and the safety in pregnancy is unknown. HEV management is only supportive, as ribavirin is contraindicated due to teratogenicity.

Globally, HCC is highly prevalent resulting in 5% of all cancers. In Africa, HCC is the 4th most common cancer on the continent and 12 African countries belong to the 25 countries with the highest HCC burden. Males have a higher burden due to a higher HBV prevalence[28]. In Africa, other common HCC risk factors includes; HCV, Aflatoxin (causes p53 mutation and is synergistic with HBV), a dietary iron overload, and to lesser extent alcohol, tobacco, and obesity/ NASH[29]. Risk factors vary from one region to another, depending on lifestyle, habits, food intake, and surrounding infections. HCC prevention requires knowledge of these risk factors and methods to avoid them[28]. Furthermore, HBV vaccinations will prevent new HBV infections and with that the natural course of disease resulting in cirrhosis and HCC. Additionally, antiviral therapy for HBV and HCV infected patients can also prevent HCC cases.

Due to the high rate of HCC in certain risk groups surveillance is cost-effective in reducing mortality. In Africa, several barriers hamper surveillance; the underlying liver disease is undiagnosed, symptoms are absent combined with low community awareness, and poverty hampers surveillance. HCC surveillance is effective in lowering the HCC prevalence among HBV infected patients who were diagnosed and treated in SSA[30]. Therefore, more focus towards surveillance is needed and highly recommended for patients who have cirrhosis in Child-Pugh A, B, and C awaiting a liver transplant. Monitoring intervals should be dictated by rate of tumour growth and tumour incidence in the targeted population, but 6-monthly intervals are reasonable and cost-effective[31]. A national surveillance should be present to record and report HCC cases. Currently, data can be underestimated since many liver-related deaths are not identified as HCC.

The survival rate of patients with an HCC can range from 3 months up to over 5 years depending on the stage of the cancer[31]. Factors to consider in HCC management are; stage, health-care access, the availability of facilities, and patient's performance status. Patients in the early stage of the disease are eligible for a hepatic resection, the standard of care for primary liver cancer. Patients can also receive a liver transplant with the possibility of a recurrent HCC, a unique condition due a combination of the systemic nature, the immuno-compromised state, and the immune maintenance phase of the transplant graft. Another option for early stage HCC is image-guided percutaneous ablation. Ablation is potentially curative, minimally invasive, and easily repeatable for recurrence. Timely identification of HCC should be encouraged to ablative therapy is still possible.

TACE is recommended as a first line non-curative therapy for non-surgical patients with large/multifocal HCC who do not have vascular invasion or extrahepatic spread[31]. TACE, regional therapy which stems from the difference in the dual blood inflow supply via the portal vein and hepatic artery between normal liver parenchyma and HCC, can be used as neoadjuvant therapy to reduce the tumour size, including tumour necrosis, and preventing dissemination during surgery of resectable HCC cases. TACE has both selective ischemic and therapeutic effects on HCC. Contraindications for TACE are an intractable systemic infection, Child-Pugh C or the presence of hepatofugal portal flow. Additionally, patients with cardiac/renal failure, impaired liver function, clinically relevant ascites, or a transjugular intrahepatic portosystemic shunt are not suitable. In 50% of cases de TACE procedure is complicated by a post embolization syndrome from which recovery usually takes place in 7-10 days. Systemic therapy can be performed in a more advanced stage of HCC including anti-angiogenics in the first line (sorafenib/lenvatinib/folfox) and second-line setting (regorafenib/cabozantinib/ramucirumab). Only folfox achieved cost-effectiveness in a LMIC setting.

Reducing mortality from hepatitis related HCC is an impact indicator for the elimination of viral hepatitis by 2030. There is still a lack of recognition that HCC is the 20-30 years of delay from a viral hepatitis infection. Therefore, surveillance and early detection of viral hepatitis and HCC are essential so as adding HCC as a priority to the research agenda in Africa. The development of a national database can accelerate data generation and facilitate regional and global documentation. Furthermore, collaboration and global partnerships are important in developing research capacity but also provide access to early diagnosis, and innovations in treatment and prevention. Currently, effective treatment for those with an advanced disease is lacking and costs are catastrophic. A solid strategic plan is needed for the use of limited human and financial resources. Evidence based advocacy can start the dialogue with policy makers, mobilize political and community action for a change.

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

The global NAFLD prevalence ranges from 13-32% with the highest burden in the middle-east region[32]. NAFLD is a complex disease trait of genetic and environmental modifiers resulting in non-alcoholic steatohepatitis (NASH). NASH is a growing and common cause of liver-related morbidity and mortality and projected to become the leading indication of liver transplantations in the US. Moreover, it will be the leading cost of fibrosis, liver failure, and liver cancer.

The natural history of NAFLD is the progression towards NASH (12-40%), while in some case rapid progression towards fibrosis (F3) occurs (8%). A biopsy showing inflammation and ballooning injury of the hepatocyte can confirms NASH[33]. The change of NASH with significant fibrosis is higher among individuals aged >50 years, from Hispanic origin, with obesity or diabetes mellitus, with an AST>40, AST/ALT ration ≥1, FIB-4>2.67, and FS kPa>8.5.

Currently, no approved pharmacotherapies for NASH are available. Drugs are, however, in the pipeline at phase II and phase III clinical trials, which includes Elafibranor, Obeticholic acid (promising results), Selonsertib (disappointing results), and Cenicriviroc. These drugs (GLP1 analogs and SGLT2 inhibiotors) are likely to be hepatoprotective in NASH. Pharmacological therapies should be reserved for patients with NASH and fibrosis since these patients are at risk for liver failure and HCC. Patients with NASH should always be referred to expertise centres to be evaluated for ongoing clinical studies. Other NAFLD therapy options are lifestyle changes towards a healthy diet and habitual physical activity, a 7-10% weight loss in obese patients is beneficial[34]. Patient with NAFLD should not consume heavy amounts of alcohol.

There is insufficient data regarding the tolerable amount of alcohol. The prognosis is worse with more drinking >1.5 drinks/day, however completely stopping does not have a better outcome as drinking 0.5-1 glass per day[35]. The use of coffee can be recommended, which showed improvement of fibrosis and there is a dose response rate with coffee and the occurrence of NAFLD[36]. Moreover, bariatric surgery is optional in obese individuals who failed lifestyle changes and pharmacotherapies.

CONCLUSION

HBV and HCV are highly prevalent on the African continent resulting in a higher burden of disease as HIV, TBC, and malaria combined. While several countries developed successful HCV elimination programs the HBV elimination is moving slow. Diagnosis rates of patients with HBV are low and nowhere close to the WHO elimination goals. Additionally, the HBV monitoring and care algorithm is very complex and not suitable for the African continent. Importantly, the birth dose should be increased to prevent new HBV infections.

Prevention of HBV infections is key in order to reduce HCC prevalence, the 4th most common cancer on the continent. Reducing mortality from hepatitis related HCC is an impact indicator for the elimination of viral hepatitis by 2030. Therefore, surveillance and early detection of viral hepatitis and HCC are essential so as adding HCC as a priority to the African research agenda. The third edition of COLDA will be held in Senegal on the 10th of September 2020. This edition focusses more on protecting both mothers and children from viral hepatitis.

REFERENCES

1. Global Hepatitis Report 2017. Geneva: World Health Organization; 2017. Geneva2017. Report No.: CC BY-NC-SA 3.0 IGO.
2. Stanaway JD, Flaxman AD, Naghavi M, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet 2016;388:1081-8.
3. Ward JW, Wiktor SZ, Cooke GS. Launch of the Coalition for Global Hepatitis Elimination: a recommendation of the Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol 2020;5:8-10.
4. World Health Organization t. Progress report on HIV, viral hepatitis and sexually transmitted infections 2019. Accountability for the global health sector strategies, 2016–2021. Geneva: World Health Organization2019. Report No.: WHO/CDS/HIV/19.7.
5. Polaris Observatory HCVC. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2017;2:161-76.
6. El-Akel W, El-Sayed MH, El Kassas M, et al. National treatment programme of hepatitis C in Egypt: Hepatitis C virus model of care. J Viral Hepat 2017;24:262-7.
7. Umutesi G, Shumbusho F, Kateera F, et al. Rwanda launches a 5-year national hepatitis C elimination plan: A landmark in sub-Saharan Africa. J Hepatol 2019;70:1043-5.
8. Shiha G, Soliman R, Mikhail NN, Easterbrook P. Educate, Test and Treat Model towards elimination of hepatitis C infection in Egypt: Feasibility and effectiveness in 73 villages. J Hepatol 2019.
9. Shiha G, Metwally AM, Soliman R, Elbasiony M, Mikhail NNH, Easterbrook P. An educate, test, and treat programme towards elimination of hepatitis C infection in Egypt: a community-based demonstration project. Lancet Gastroenterol Hepatol 2018;3:778-89.
10. Desalegn H, Johannessen A. Response to Non-invasive fibrosis markers for chronic hepatitis B in sub-Saharan Africa. Liver Int 2017;37:1739.
11. Aberra H, Desalegn H, Berhe N, et al. The WHO guidelines for chronic hepatitis B fail to detect half of the patients in need of treatment in Ethiopia. J Hepatol 2019;70:1065-71.
12. Tordrup D, Hutin Y, Stenberg K, et al. Additional resource needs for viral hepatitis elimination through universal health coverage: projections in 67 low-income and middle-income countries, 2016-30. Lancet Glob Health 2019;7:e1180-e8.
13. Pedrana A HJ, Schröder S, Scott N, Wilson D, Kuschel C, Auffegger L, Hellard M. . Eliminating Viral Hepatitis: The investment Case World Innovation Summit for Health, 2018. Doha, Qatar 2018.
14. Stephanie Popping DB, Charles Boucher, Mark van der Valk, Manal El-Sayed, Olafsson Sigurour, Vana Sypsa, Timothy Morgan, Amiran Gamkrelidze, Constance Mukabatsinda, Sylvie Deuffic-Burban, Michael Ninburg, Jordan Feld, Margaret Hellard, John Ward. The global campaign to eliminate HBV and HCV infection: International Viral Hepatitis Elimination Meeting and core indicators for development towards the 2030 elimination goals. Jorunal of Virus Eradication 2019;5:60-6.
15. Gupta N, Mbituyumuremyi A, Kabahizi J, et al. Treatment of chronic hepatitis C virus infection in Rwanda with ledipasvir-sofosbuvir (SHARED): a single-arm trial. Lancet Gastroenterol Hepatol 2019;4:119-26.
16. Childs K, Davis C, Cannon M, et al. Suboptimal SVR rates in African patients with atypical Genotype 1 subtypes: implications for global elimination of Hepatitis C. J Hepatol 2019.
17. S. Popping* SF, AYM Howe , A. de Salazar, VC Di Maio, ESE Tay, C. Rodrigo, E. Cunningham, M. Kjellin, J. Sfalcin, P. Gomes, M. Poljak, M. Lunar, M. Sayan, O. Mor, D. Salmon, R. Usubillaga, C. Seguin-Devaux, A. Soulier , A. Lloyd , J. Grebely, J. Lennerstrand, R. Kaiser, P. Zhigalkina, V. Chulanov, RJ de Knegt, M. Douglas, F. Ceccherini-Silberstein, R. Harrigan, F. Garcia ,C. Boucher, JM Pawlotsky On behalf of the contributing members of the SHARED database. The global prevalence of resistance-associated substitutions (RAS) in "unusual" HCV subtypes AASLD the Liver meeting Boston MA2019.
18. Smedile A, Farci P, Verme G, et al. Influence of delta infection on severity of hepatitis B. Lancet 1982;2:945-7.
19. Smedile A, Dentico P, Zanetti A, et al. Infection with the delta agent in chronic HBsAg carriers. Gastroenterology 1981;81:992-7.
20. Daw MA, Daw AM, Sifennasr NEM, et al. The Epidemiology of Hepatitis D Virus in North Africa: A Systematic Review and Meta-Analysis. ScientificWorldJournal 2018;2018:9312650.
21. Stockdale AJ, Chaponda M, Beloukas A, et al. Prevalence of hepatitis D virus infection in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health 2017;5:e992-e1003.
22. Keane E, Funk AL, Shimakawa Y. Systematic review with meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa. Aliment Pharmacol Ther 2016;44:1005-17.
23. Shimakawa Y, Lemoine M, Njai HF, et al. Natural history of chronic HBV infection in West Africa: a longitudinal population-based study from The Gambia. Gut 2016;65:2007-16.

REFERENCES

24. Flynn PM, Mirochnick M, Shapiro DE, et al. Pharmacokinetics and safety of single-dose tenofovir disoproxil fumarate and emtricitabine in HIV-1-infected pregnant women and their infants. Antimicrob Agents Chemother 2011;55:5914-22.
25. American College of O, Gynecologists. ACOG Practice Bulletin No. 86: Viral hepatitis in pregnancy. Obstet Gynecol 2007;110:941-56.
26. Samer El-Kamary KS, Debra Birnkrant, FDA Combined clinical review, cross-discipline team leader review - Sofosbuvir/Ledipasvir for peadiatric patients: Gilead sciences October, 2017.
27. Kim JH, Nelson KE, Panzner U, Kasture Y, Labrique AB, Wierzba TF. A systematic review of the epidemiology of hepatitis E virus in Africa. BMC Infect Dis 2014;14:308.
28. Yang JD, Mohamed EA, Aziz AO, et al. Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium. Lancet Gastroenterol Hepatol 2017;2:103-11.
29. Ladep NG, Lesi OA, Mark P, et al. Problem of hepatocellular carcinoma in West Africa. World J Hepatol 2014;6:783-92.
30. Cohen D, Shimakawa Y, Ndow G, et al. [Prevention of liver fibrosis and liver cancer linked to hepatitis B virus in Africa: the Prolifica study] Prevention de la fibrose et du cancer du foie lies au virus de l'hepatite B en Afrique - Le projet Prolifica. Med Sci (Paris) 2019;35:431-9.
31. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol 2018;69:182-236.
32. Younossi ZM, Blissett D, Blissett R, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology 2016;64:1577-86.
33. Kleiner DE, Brunt EM, Van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology 2005;41:1313-21.
34. European Association for the Study of the L, European Association for the Study of D, European Association for the Study of O. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016;64:1388-402.
35. Hajifathalian K, Torabi Sagvand B, McCullough AJ. Effect of Alcohol Consumption on Survival in Nonalcoholic Fatty Liver Disease: A National Prospective Cohort Study. Hepatology 2019;70:511-21.
36. Romero-Gomez M, Zelber-Sagi S, Trenell M. Treatment of NAFLD with diet, physical activity and exercise. J Hepatol 2017;67:829-46.

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