SASLT
الجمعية السعودية لأمراض وزراعة الكبد
Saudi Society for the Study of Liver Disease and Transplantation

الجمعية تحت إشراف
الهيئة السعودية للتخصصات الصحية
Saudi Commission for Health Specialties

4th Issue

SASLT NEWSLETTER

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A Farewell Note

EVERY END IS A NEW BEGINNING

It's been a year since we launched this newsletter, and to all of you who began this journey with us, we bid you a fond farewell. Time moves fast when we are in a period of flux. In this short space of time we have learnt much from our readers who lent us their feedback, from the experts who voiced their learned opinions, and from the researchers who contributed with their innovative ideas. When we were handed this task, our desire was to highlight the changes, strides and achievements of the hepatology and liver transplant community, by featuring what we believed was relevant to the local practitioners. It has been a joy to follow and participate in the local trends and events, and to pour over homegrown liver-related publications. We followed with excitement as SASLT found a new footing and held its own annual scientific meeting. We witnessed the growing anticipation as the hepatology community increased in number and strength, and celebrated as the trend of our research grew in character and quality. As we observe these many changes, we believe also in the commitment for change at this newsletter. A new team must take over its course, bringing with it its new ideas and priorities. And like we said before, SASLT will remain true to its founding mission, but how it intends to inspire and grow will continue to evolve. Truly, success lies in the effort!

Dr. Faisal M. Sanai

A KEY MILESTONE

The start of the transplant hepatology fellowship program in Saudi Arabia

Dr. A. Almoaid

Dr. W. Alghamdi

Dr. A. Albenmousa

Dr. F. Sanai

The practice of hepatology in the Kingdom has significantly evolved over the last few decades. With the expansion of liver transplant centers, the demand for transplant hepatologists is growing. Furthermore, the need for hepatologists across the Kingdom has never been adequately met. Gastroenterology trainees may not get sufficient hepatology exposure, and exposure to liver transplantation is not a requisite of their training. Fellowship training in hepatology has been limited to overseas programs. The success in the core gastroenterology training and the presence of well-trained physicians in various gastroenterology sub-specialties has opened the door wide for subspecialty training. With generous governmental support, many hospitals and centers within the country are of world class quality.

> *"The aim was to reduce dependence on overseas fellowships, and to provide & develop the necessary tools for homegrown training"*
>
> *- Dr. Faisal Sanai*

In 2021, the adult transplantation hepatology fellowship program was commissioned by the SCFHS. "There have been a growing chorus of calls for such a program to be started in lieu of the increasing number of patients undergoing liver transplantation within the country, along with the growing recognition that there existed a severe shortage of accredited physicians particularly within the transplantation centers. The aim was to reduce dependence on overseas fellowships, and to provide and develop the necessary tools for homegrown training" says Dr. Faisal Sanai, the chair of the founding scientific committee. Two centers have been accredited by SCFHS for this program.

With over 300 liver transplantations being performed annually, King Faisal Specialist Hospital and Research Center (KFSHRC) in Riyadh is among the leading liver transplant centers worldwide. "The referral for patients with decompensated cirrhosis and hepatocellular carcinoma in need of transplantation has notably increased, and the need for locally accredited liver

transplant training has become clear. The presence of competent transplant hepatologists across the Kingdom will really help to facilitate patients care outside the transplant centers, limiting the need for patients to travel outside their cities" says Dr. Ali Albenmousa, a transplant hepatologist, and the program director for transplant hepatology fellowship at KFSHRC. "It was exciting to start the program; the presence of fellows and residents in any program will boost the education and patient care". The program at KFSHRC has two seats for applications each year. Applicants need to have Saudi Board of Gastroenterology certification or equivalent qualification.

> *"I had a wonderful year of training which just ended"*
>
> *- Dr. Abdullah Almoaid*

While KFSHRC may fund the applicants, this is not guaranteed. "We encourage candidates to have a sponsor at the time of their application". The beginning of any new programs is not without difficulties. "We faced no major challenges, however there were some gaps in registration and evaluation that we addressed" said Dr. Albenmousa.

In January 2022, Dr. Abdullah Almoaid became the first Saudi fellow to be enrolled in this fellowship program at KFSHRC. Dr. Amnah Alhanea, from United Arab Emirates, also enrolled at the same time and both graduated at the end of 2022. "I had a wonderful year of training which just ended a few days ago" said Dr. Almoaid. "KFSHRC has all what is needed to be a comprehensive hepatology and liver transplant training program, considering the number of experts in various specialties, the large number of patients, and hence the unlimited exposure". Dr. Almoaid is now preparing to return to King Fahad Hospital in Madinah, where he will take care of liver disease patients.

> *"It was exciting to start the program; the presence of fellows and residents in any program will boost the education and patient care".*
>
> *- Dr. Ali Albenmousa*

While this current program is built to accredit liver transplantation training, the vast majority of patients with liver disease will never require liver transplantation. It is not clear if the national demand for hepatologists can be met with the two accredited training centers. "It may just be able to meet the demand for transplant hepatologists if we consider only the 3 or 4 transplant centers countrywide. However, it simply will not be sufficient if we take into consideration the dire need of non-transplant hepatologists across the length and breadth of the country" says Dr. Sanai. He adds "What we most urgently require is a comprehensive hepatology training program that will allow for the

> *"There is an urgent need for accredited structured adult hepatology training programs independent of the liver transplant training centers"*
>
> *- Dr. Waleed Alghamdi*

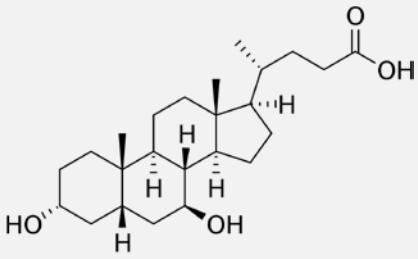
adequate management of all those patients who have a liver disease but may not necessarily need liver transplantation. As hepatologists across the country are well aware, this forms the vast bulk of their work. But it doesn't make sense to start a

hepatology training program, and a separate one for liver transplantation. Perhaps this Adult Transplant Hepatology Fellowship Program ought to be restructured to allow for core hepatology training, with the option of additional liver transplantation training made available in key centers where this facility is available. This is how I would have designed it". Dr. Waleed Alghamdi, a transplant hepatologist at King Abdulaziz University Hospital concurs with Dr. Sanai. "Hepatology has been considered a small component within the huge practice scope of gastroenterology specialty. The Kingdom of Saudi Arabia has witnessed a paradigm shift in the field of hepatology practice due to many variables. With the expansion of patients with liver disease requiring specialized care, hepatology care comes into play, which we know would improve outcomes of these patients" says Dr. Alghamdi. He adds "There is an urgent need for an accredited, structured, adult hepatology training program, independent of the liver transplant training centers. We need to meet the rising demand of care for liver diseases amidst the global obesity, and subsequently, non-alcoholic steatohepatitis epidemic." How such expectations are met will obviously define the course of this program, and how it will evolve in the future. Nonetheless, today it is clearly a step in the right direction, wherein the country has placed obvious faith in being able to harness the existing local expertise and provide cutting-edge home-grown training for sub-specialty programs.

Dr. Majid Alsahafi

Efficacy of ursodeoxycholic acid for primary biliary cholangitis: Experience from a tertiary care centre in Saudi Arabia

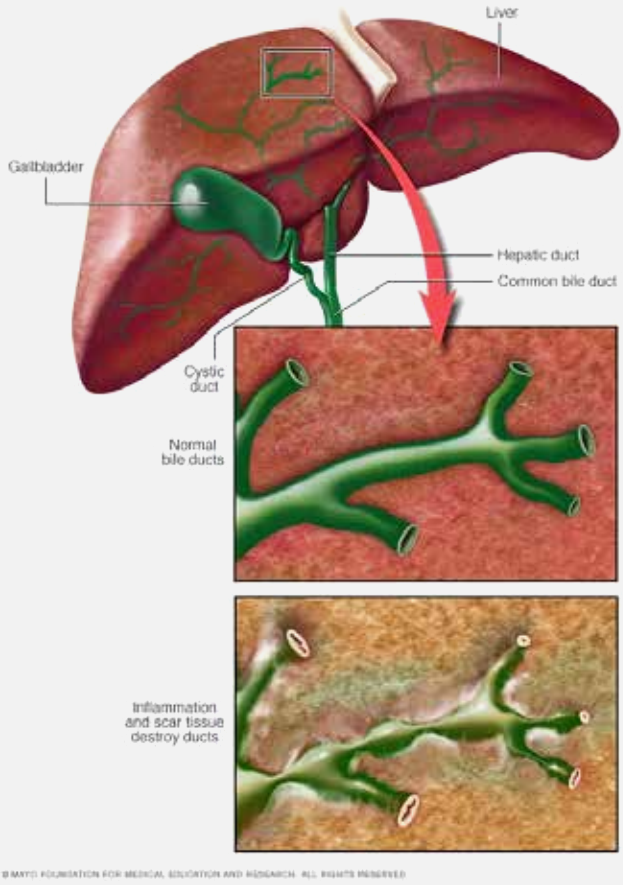
AlWabel AH, et al. Saudi J Gastroenterol. 2022 Feb 23. DOI: 10.4103/sjg.sjg_445_21.



Primary biliary cholangitis (PBC) is a progressive autoimmune cholestatic liver disease characterized by the destruction of the small intralobular bile ducts, leading to chronic non-suppurative destructive cholangitis, with eventual bile duct loss, fibrosis, and cirrhosis. In this study, AlWabel and his colleagues report the first study from Saudi Arabia on the clinical characteristics and treatment response to ursodeoxycholic acid (UDCA) in patients with PBC. They identified 30 patients with PBC followed over ten years.

The mean age was 46 years ± 11.7, with a female gender predominance of 93%. Pruritus was reported in 90% (n = 27) of the patients. 23 (77.7%) patients underwent liver biopsy, and all showed histological features suggestive of PBC. Cirrhosis was documented in 30% (n = 9) of the patients at baseline, and 86.7% (n = 26) of the patients were positive for antimitochondrial antibodies. The biochemical response rates to UDCA based on Paris I, Paris II, Barcelona, and Toronto criteria were 73.3, 40, 56.7, and 53.3%, respectively. Fatigue was underreported compared to other reports, which may in part be related to the retrospective nature of the study. The study's main limitations were the small sample size and having data only from a single center.

The authors concluded that UDCA was inadequate as a treatment option, in agreement with other international studies. The investigators advocate that multicentre studies on PBC prevalence and treatment strategies in Saudi Arabia are needed. Further research is warranted in patients with sub-optimal response to UDCA, and the role of fibrates and obeticholic acid.

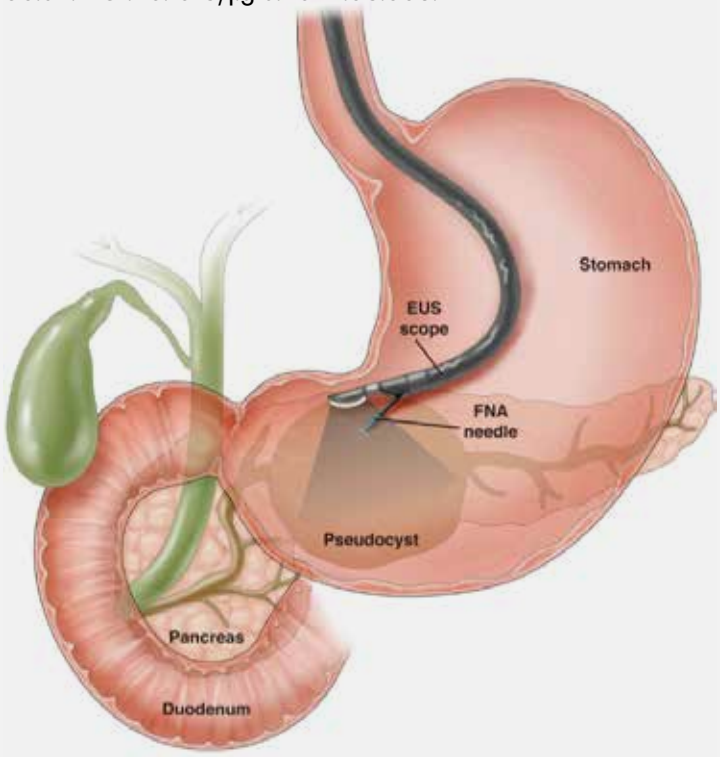


Randomized trial comparing general anesthesia with anesthesiologist-administered deep sedation for ERCP in average-risk patients

Alzanbagi AB, et al. Gastrointest Endosc. 2022 Dec;96(6):983-990.e2. DOI: 10.1016/j.gie.2022.06.003.

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a complex endoscopic procedure with potentially severe adverse events, including mortality. The number of ERCPs has steadily increased in recent years, offering more therapeutic interventions than before. While routine sedation in ERCP improves the procedure's efficiency, success, and comfort, practices vary internationally. Whether monitored anesthesia care (MAC) or general anesthesia (GA) is better for ERCP in patients at average risk for sedation is unexplored. Hence, Alzanbagi and colleagues performed a randomized trial comparing the safety and efficacy of MAC with GA in patients at average risk for sedation undergoing ERCP.

Patients with the American Society of Anesthesiologists (ASA) class III were randomly assigned to undergo ERCP with MAC or GA at a tertiary referral center. Of 204 randomized, 203 patients were evaluated for the primary outcome, which was a composite of hypotension, arrhythmia, hypoxia, hypercapnia, apnea, and procedural interruption or termination defined as sedation-related adverse



and procedural interruption or termination defined as sedation-related adverse events (SRAEs). SRAEs developed in 35% of the MAC cohort (34/96) versus 9% in the GA cohort (10/107), which was statistically significant (P <0.001). None of the ERCP procedures was terminated in either group. Using GA improved endoscopist and patient satisfaction (P < 0.001). The study's main limitations were the adoption of procedure interruptions as SRAEs, and airway maneuvers needed to be standardized as some anesthesiologists may have performed more maneuvers than others.

The authors conclude that GA is safe with fewer SRAEs than MAC in patients with ASA scores III undergoing ERCP. Besides prolonging induction time, using GA does not change the procedural success or ERCP-related adverse events and offers greater endoscopist and patient satisfaction. The authors advocate that further studies with a larger sample size focusing on procedural time, ERCP-related adverse events, and cost-effectiveness are warranted to ascertain the routine use of GA in average-risk patients.

Attitudes Toward Organ Donation in an Arab-Based Population

Almubark RA, et al. Transplant Proc. 2022;54:2063-2068.
DOI: 10.1016/j.transproceed.2022.08.017.

Commitment to organ donation may vary among willing younger and older adults. Only 3 in 1000 individuals die in a way that permits deceased organ donation. In Saudi Arabia, a new regulation was implemented to allow the registration of organ donors. Almubark and colleagues studied attitudes toward organ donation. This was a cross-sectional survey of a representative sample of adults from all 13 regions in Saudi Arabia (Al Jouf, Northern Borders, Tabuk, Hail, Al Madinah, Al Qassim, Makkah, Riyadh, Eastern Province, Al Baha, Asir, Jizan, and Najran).

Of the 4217 individuals contacted, 3120 respondents (1846 younger and 1274 older) completed the survey, with a response rate of 74%. The study included equal numbers of males and females. More than half of the respondents had a diploma or bachelor's degree. Although 54% of younger and 47% of older respondents expressed support for organ transplantation, 49% of younger and 35% of older respondents wanted to donate their organs. Furthermore, only 4% of younger and 3% of older respondents had registered in the national donor database. Knowledge sources that were most likely to influence attitudes toward organ donation for younger and older respondents, respectively, were physician/health care workers (58% and 55%), family members (29% and 26%), scientist/researchers (29% and 22%), and religious scholar (16% and 23%).

The authors' results seem to back up what was previously known about this area. These results highlight the sources of knowledge that help increase commitment toward organ donation and are consistent with other studies that emphasize education and informing the general population about the organ donation process. Despite the large sample size, the authors cannot rule out sampling bias in this study.

In conclusion, although many younger and older adults are willing to donate, few are registered donors. The findings highlight the influential sources of knowledge for younger and older adults that can be implemented in future tailored interventions.

Dr. Mona H. Ismail

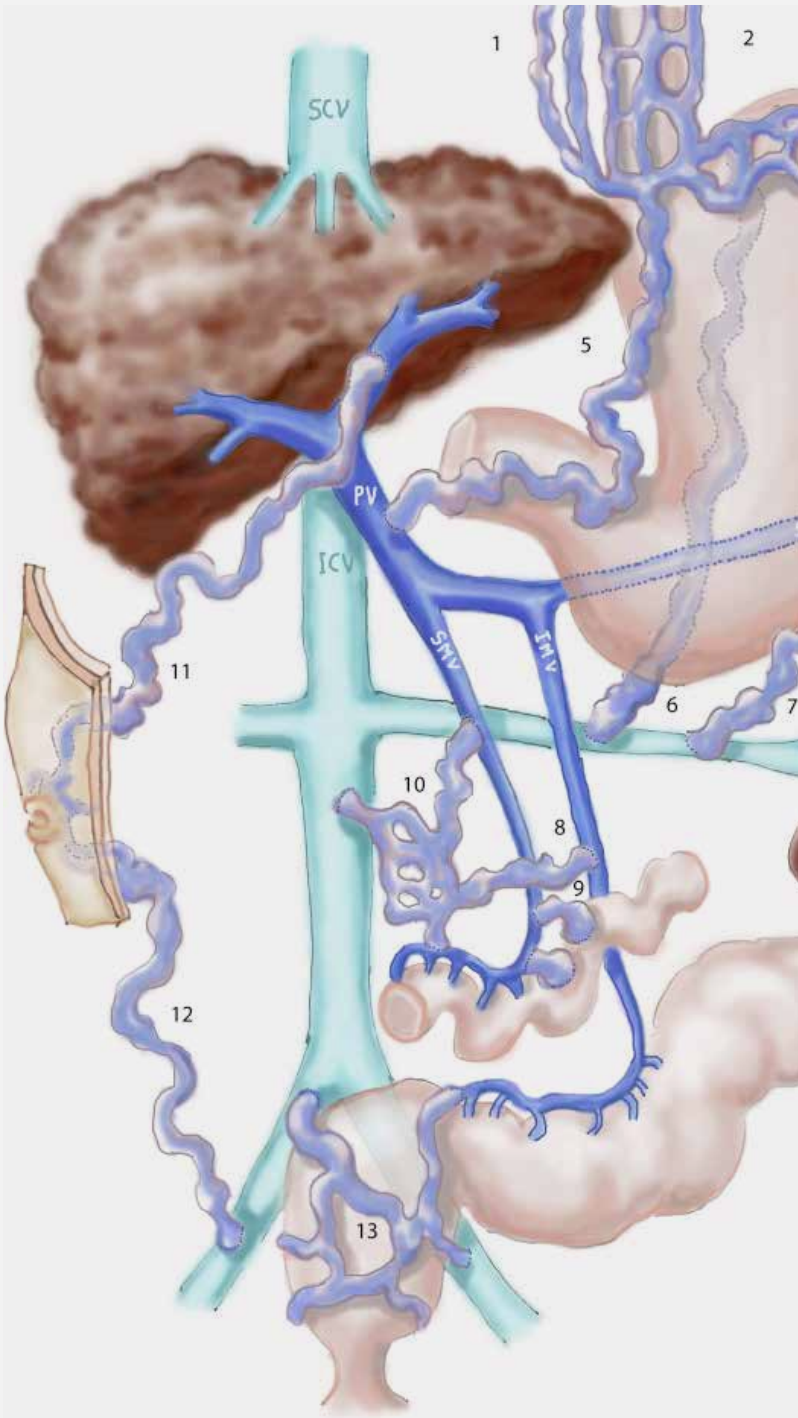
Concurrent large spontaneous portosystemic shunt embolization for the prevention of overt hepatic encephalopathy after TIPS: A randomized controlled trial

Lv Y, et al. Hepatology. 2022;76:676–688. https://doi.org/10.1002/hep.32453

Transjuglar Intrahepatic Portosystemic Shunt (TIPS) is frequently used to treat complications of portal hypertension in cirrhotic patients including variceal upper gastrointestinal bleeding and refractory ascites and/or hepatic hydrothorax. One feared complication post TIPS is recurrent overt hepatic encephalopathy (HE), which is more likely to happen in patients with pre-existing large spontaneous portosystemic shunt (SPSS).

To examine the benefit of concurrent embolization of SPSS at the time of TIPS insertion, Lv and colleagues conducted a randomized controlled trial on 56 patients with cirrhosis and large SPSS who were planned to go for TIPS insertion. Subjects were randomized to receive TIPS alone (control group) or TIPS plus simultaneous SPSS embolization (experimental group). The primary endpoint was the incidence of overt HE post intervention.

Twenty-nine patients in the control group and 27 patients in experimental group were followed up for a median of 24 months after successful TIPS with or without SPSS embolization. Overt HE occurred in 15 patients (51.7%) in control group and in six patients (22.2%) in the



experimental group. The 2-year cumulative incidence of overt HE was significantly lower in the experimental group compared with the control group (21.2% vs. 48.3%; HR, 0.38; 95% CI, 0.15–0.97; p = 0.043). The absolute risk reduction was 27% and the number needed to treat was almost 4 patients to prevent 1 overt HE. There was no significant difference in the incidence of recurrent bleeding between experimental and control groups (15.4% vs 25.1%, p=0.522) as well as shunt dysfunction (12.3 % vs 18.6%, p= 0.593). The mortality was higher in the embolization group (15.0 vs 6.9%) however, the difference not was statistically significant (p= 0.352).

Authors concluded that in patients with cirrhosis going for TIPS insertion, concurrent embolization of large SPSS reduces the risk of overt HE without increasing complications, and the number needed to treat was 4.

These findings might support the concurrent embolization of large SPSS at time of TIPS particularly for patients who are not eligible for liver transplantation, or those who have no donors where TIPS is a treatment option for them. The risk of overt HE is an important consideration against doing TIPS in cirrhotic patients since it affects their quality of life and increases the risk of falls with subsequent injuries, in addition to the substantial increase in cost to treat HE episodes. Having a relatively easy and economical prophylactic intervention will allow more utilization of TIPS for treatment of serious complications of portal hypertension. This study however, is small and not blinded, and having larger, multicenter, randomized studies aiming towards a longer duration of follow up will help to strengthen the evidence.

Two-year risedronate treatment for osteoporosis in patients with esophageal varices: A non-randomized clinical trial

Santos LAA, et al. Hepatol Int. 2022;16:1458–67.
https://doi.org/10.1007/s12072-022-10366-z

Osteoporosis is very common in patients with chronic liver diseases. Bisphosphonates are the most frequently used medication for osteoporosis treatment in non-cirrhotic patients. Their use however for patients with esophageal varices has been avoided due to the risk of esophagitis, which may cause variceal bleeding. Treating patients with the injectable form of bisphosphonate is an alternative, however this is challenged by prescription restrictions, need for specialized unit for infusion or injection, and the cost of treatment.

A recent study by Santos L et al, showed that oral risedronate was safe and effective medication to treat patients with osteoporosis and esophageal varices. The

study was a prospective non-randomized trial that included 51 cirrhotic patients who received risedronate 35mg weekly plus calcium and vitamin D and compared them to 51 cirrhotic patients with osteopenia receiving supplement only as the control group. The groups were similar in cirrhosis severity and endoscopic findings and all patients underwent scheduled (EGDs) esophagogastroduodenoscopies and bone mineral densitometry measurements. Patients were followed up for 2 years.

The adjusted esophagitis risk was higher in the intervention group however, none of the subjects developed upper gastrointestinal bleeding. Lumbar spine BMD increased in the intervention group (- 3.06 ± 0.71 to - 2.33 ± 0.90; $p < 0.001$) and in the control group (- 1.38 ± 0.77 to - 1.10 ± 1.05; $p = 0.012$). Femoral neck BMD did not change in the intervention group (- 1.64 ± 0.91 to - 1.71 ± 0.95; $p = 0.220$), but tended to decrease in the control group (- 1.00 ± 0.74 to - 1.09 ± 0.82; $p = 0.053$).

The major drawback of this study is the lack of randomization however, having no single episode of variceal bleeding after 2 years of treatment considerable assurance about the safety of oral bisphosphonates in cirrhotic patients. Until results of larger randomized controlled trials are available, gastroenterologists and hepatologists may consider the used of oral bisphosphonate for management of osteoporosis in selected patients with small-to-medium sized esophageal varices with no high-risk signs and with regular surveillance EGDs.

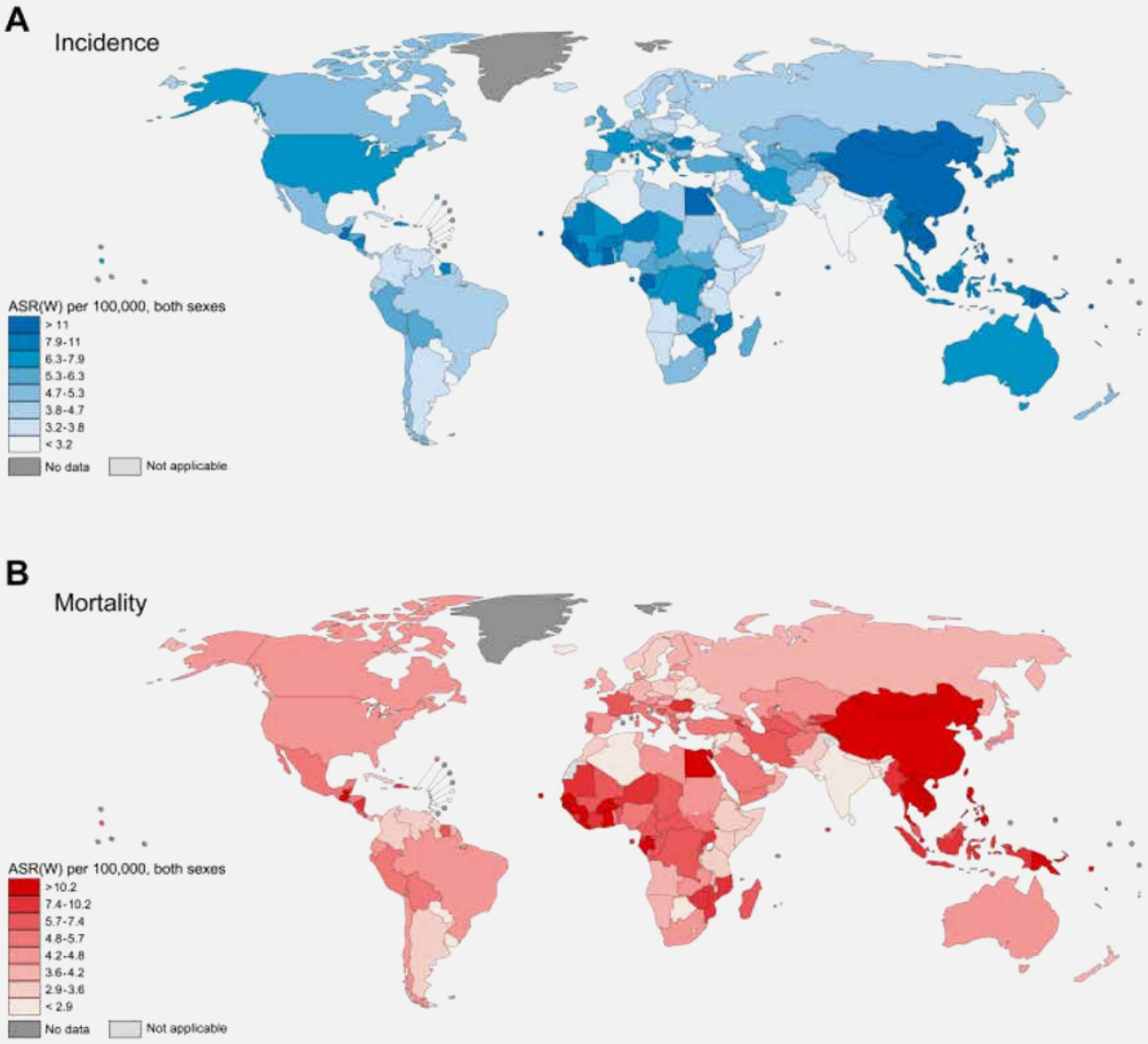
Global burden of primary liver cancer in 2020 and predictions to 2040

Rumgay H, et al. J Hepatol. 2022;77:1598-1606.
DOI: 10.1016/j.jhep.

Despite the great achievements in management of chronic liver diseases particularly chronic viral hepatitis over the last 2 decades, the burden of primary liver cancer is unfortunately on rise with some variations across the world. It was estimated that 905,700 people were diagnosed with and 830,200 people died from liver cancer globally in 2020 making it among the top three causes of cancer death in many countries.

Rumgay and colleagues recently estimated the projected burden of primary liver cancer in 2040. Data were extracted from Globocan 2020 database (an online database providing global cancer statistics and estimates of incidence and mortality from 185 countries). Age-standardized incidence and mortality rates (ASRs) per 100,000 person-years were calculated. Cases and deaths up to the year 2040 were predicted based on incidence and mortality rates for 2020 and global demographic projections to 2040.

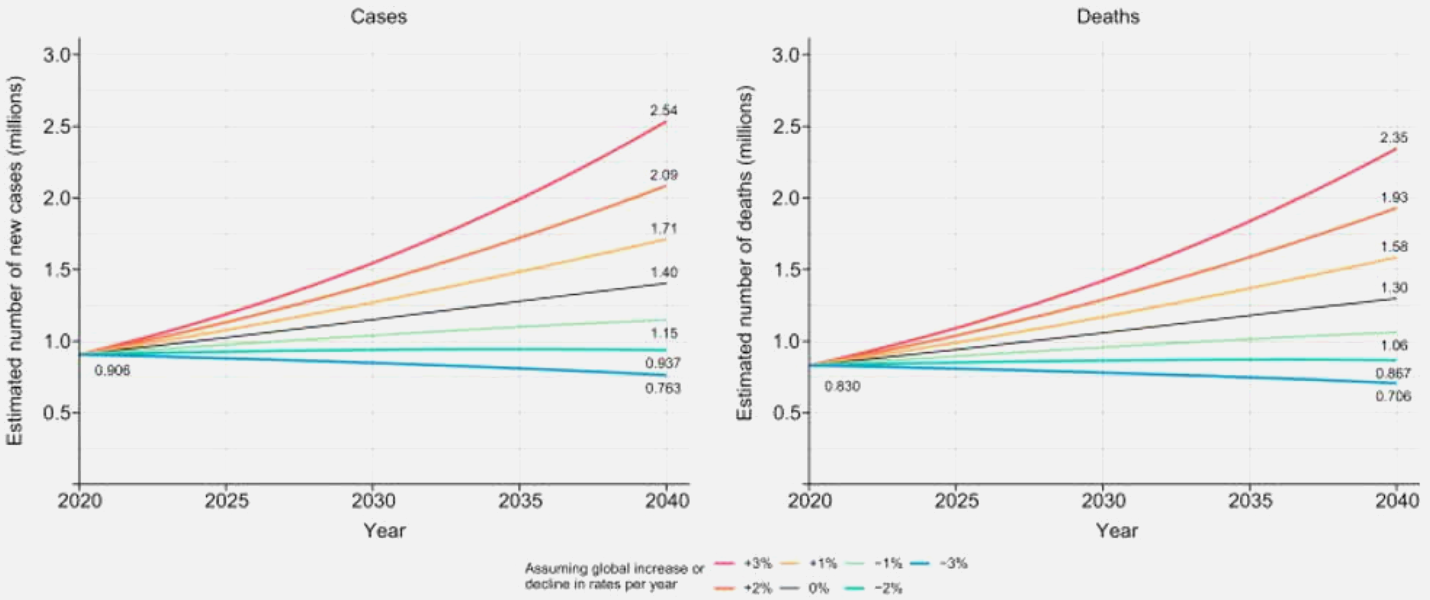
In 2020, global ASRs for liver cancer were 9.5 and 8.7 for new cases and deaths, respectively, per 100,000 people and were



highest in Eastern Asia (17.8 new cases, 16.1 deaths), Northern Africa (15.2 new cases, 14.5 deaths), and South-Eastern Asia (13.7 new cases, 13.2 deaths) (Figure 1). The number of new cases of liver cancer per year is predicted to increase by 55.0% between 2020 and 2040, with a possible 1.4 million people diagnosed in 2040. The model predicted that 1.3 million people could die from liver cancer in 2040 (56.4% more than in 2020) (Figure 2).

The main reason for this rise in liver cancer cases is the expansion of population and aging rather than increase in the incidence of risk factors. Controlling preventable risk factors like viral hepatitis B & C and aspergillus flavus contamination could potentially reduce liver cancer deaths significantly.

These data are very important for health care providers & planners since they need to adequately plan for such increases in terms of prevention and management particularly the number of liver transplantations required & the availability of organs. National programs for early detection of liver cancers as well as their risk factors may help to reduce the mortality and the need for liver transplantation. Education, screening for viral hepatitis and management of obesity are important milestones of such programs.



Dr. Ali Albenmousa

THE **Excellence** Corner

Interview with

Prof. Faleh AlFaleh

Editor

Can you describe the challenges that you faced in your journey?

Prof. Faleh AlFaleh

My earlier schooling years were generally smooth, and I avoided the many challenges that others experienced in that era. The first challenge I faced was after I completed my secondary studies in Riyadh in 1960, I was sent for university studies to Germany when I didn't speak their language. However, I was accepted in a very well-known University in Heidelberg, which is the oldest University in Germany and the very best in its field of studies. While fortunately I didn't face major problems during my studying years at the University, I consider the major challenge was when I came back to Saudi Arabia around 1978 and tried to get accepted to work in the College of Medicine at King Saud University. Much to my surprise, that despite being one of the few Saudis with Western qualifications and a specialization certificate in gastroenterology, I was rejected on the basis that I was the first Saudi graduate from Germany to work at the college, which was managed by one of the UK universities, which as a consequence preferred UK graduates. Accordingly, I decided to go and visit the Minster of Higher Education, the late Shaikh Hassan AlShaikh who, in half an hour, asked his secretary to send a letter to the university director asking him to accept my application immediately since the German degree was already recognized as an equivalent to the UK degrees.

However, my problems did not end here, and I faced several other challenges. Obviously, I was very interested in furthering research within the country and I recall how difficult it was for me to get funding for essential research from both, the Ministry of Health (as they said they didn't have enough funds) as well as from the King Abdulaziz City for Science and Technology. Unfortunately, there was no concept for research philanthropy. At that time, notable businessmen were not really interested to fund such research (in one case, a businessman conditioned his support if we can get a fatwa stating that this be considered part of Zakat).

Editor

Can you list (what you believe are) your achievements in this field?

Prof. Faleh AlFaleh

I consider my research work on viral hepatitis B and C as being amongst the most important achievements of my career, especially when my team and I convinced the Ministry of Health to start hepatitis B vaccination in 1989 for all children at birth. We were the first in the entire Arab world to implement this as part of a national health strategy, and of a few in the world that had implemented it back then. Now, and as a direct consequence of this effort, after 33 years I can look back in satisfaction that this policy helped prevent hepatitis B infection in possibly hundreds of thousands of children. I have published over 100 research articles in local and international journals within the field of gastroenterology and hepatology. This has also included publications in high end, high impact journals such as “Hepatology”. In addition, I had a pioneering role in establishing the Saudi Commission for Health Specialties, which I believe has contributed vastly towards improving the healthcare service, and in streamlining and developing of medical specialties in our country. I have also been fortunate to be in the Medical Award selection committee in the King Faisal Prize for 30 years. Finally, I was among the first of the physicians to be selected to serve in the Shoura Council in 1994.

AlFaleh (seated in front) with friends from the faculties of school of medicine from the three universities (KSU, KAUH, KFU) in 1980

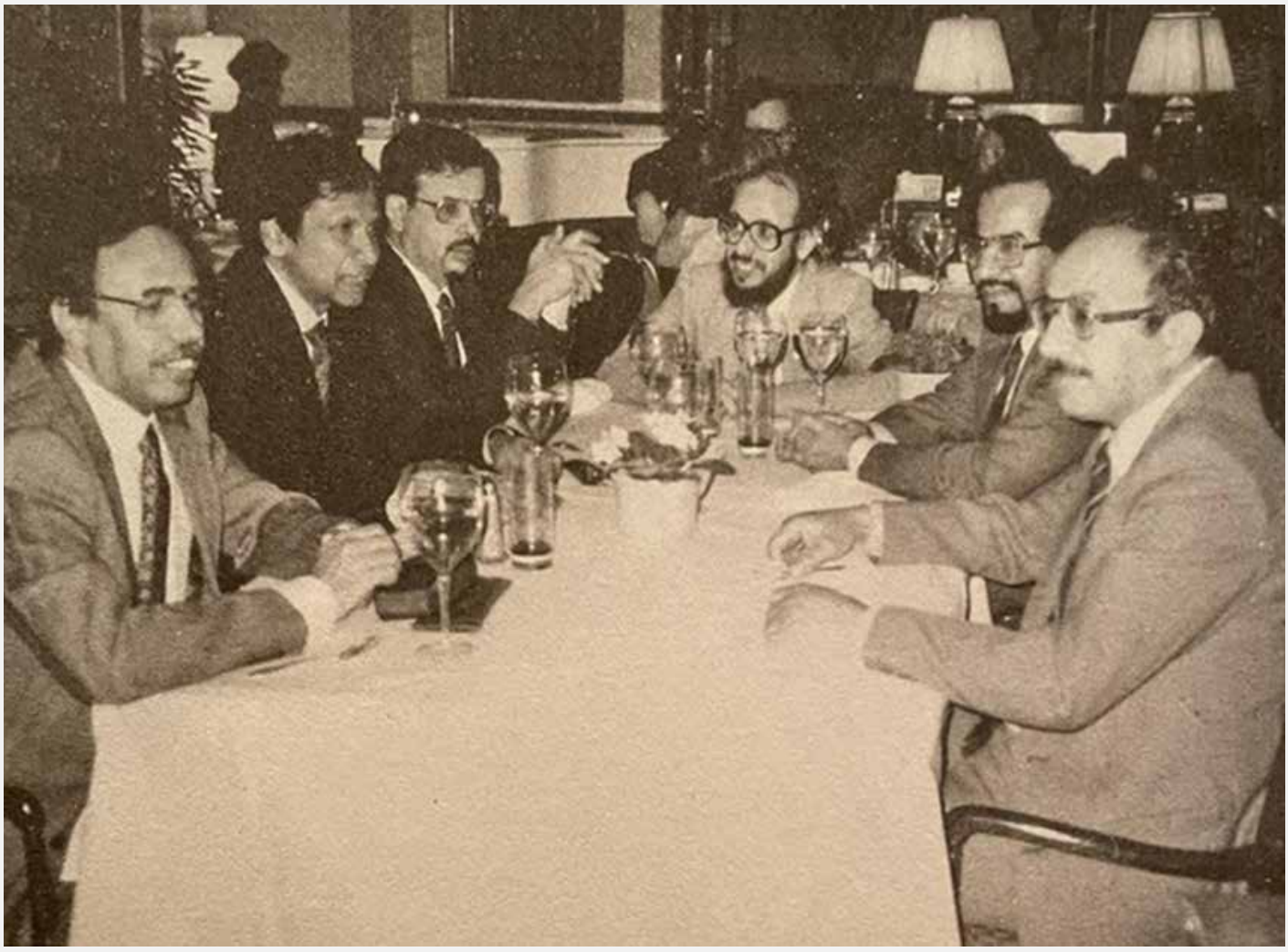
AlFaleh (first from left) with colleagues and friends

Editor

What changes would you advocate for the betterment of our goals in science?

Prof. Faleh AlFaleh

To answer this question, it is important to point out the factors that have impacted the scientific research in the medical field in our country. First, was the absence of a vision, and the political and administrative will to support medical research and scientific development. Second, I believe that we do not encourage in our educational system, a culture of critical thinking or deep research. Third, is the enduring influence of bureaucracy and financial strains on our decision makers in the academic and research institutions. Finally, and not the least, is the lack of adequate, much needed, and necessary funding to support the research community in the medical field.



Prof. AlFaleh in an international conference in the mid-1980s with colleagues from Saudi Arabia and USA

Editor

Any regrets or unfulfilled ambitions in life?

Prof. Faleh AlFaleh

No, I have lived a rich and fulfilled life and I look forward to giving more.

Editor

What message would you like to pass on to this generation of doctors and the next?

Prof. Faleh AlFaleh

I believe that one of the most important aspects that supports doctors in doing their job is how they manage their relationships with their patients; to be able to listen carefully to their cry for help, and to be patient and respectful of their needs. My message to all doctors would be to imbibe this in your practice and let it become the way how you practice medicine.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VEMLIDY has a novel mechanism of action
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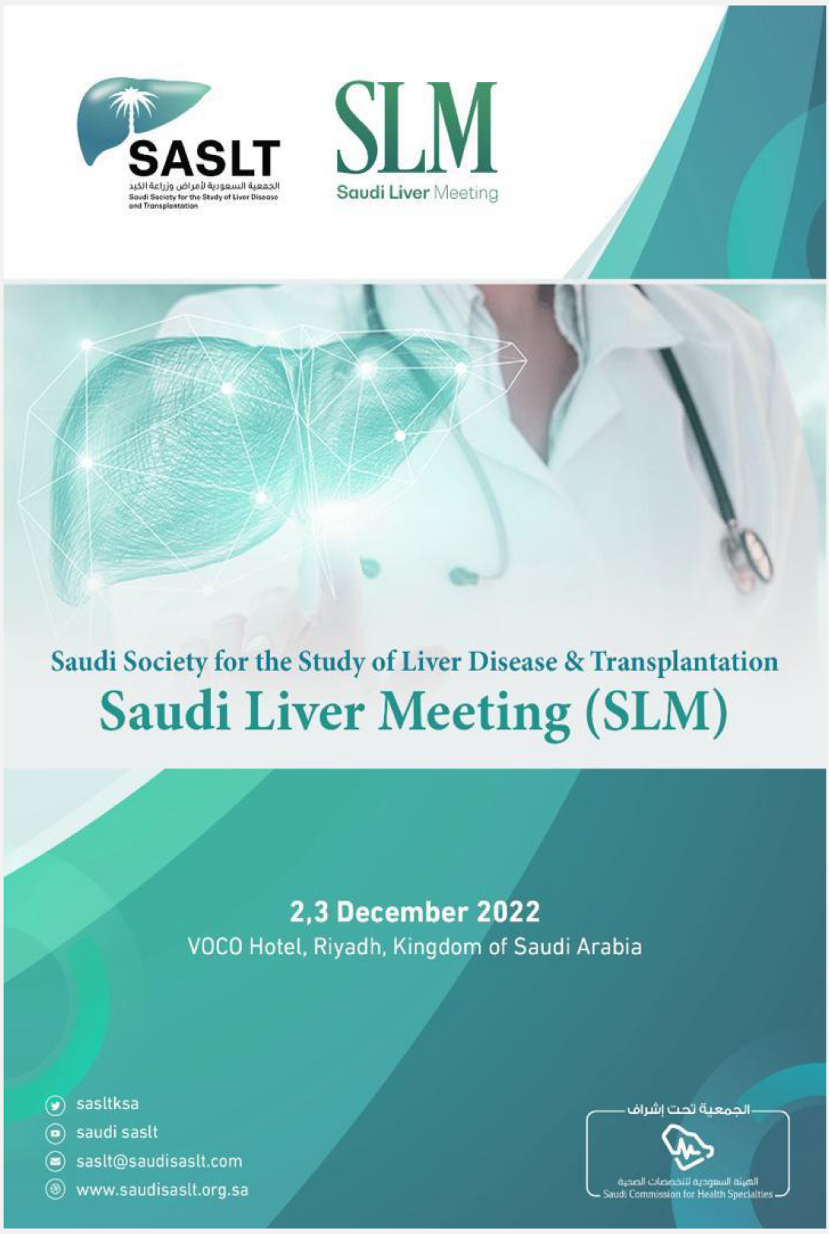
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