Klebsiella pneumoniae vs. Non-*Klebsiella pneumoniae* Pyogenic Liver Abscess

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Pyogenic liver abscess (PLA) is a common global public health problem as it contributes to 13% of intra-abdominal abscesses. With advancements in diagnostic microbiology, imaging technology, improved understanding of sepsis and critical care, and minimally invasive image-guided interventions such as percutaneous drainage (PD), clinical outcomes continue to improve; however, PLA-related mortality remains high, in the range of 10–30%. *Klebsiella pneumoniae* (KP) is the leading causative organism for PLA, followed by *Escherichia coli* (EC). *Klebsiella pneumoniae* pyogenic liver abscess (KPPLA) is associated with DM and gas formation, possibly impacting clinical outcomes.

1. Introduction

Pyogenic liver abscess (PLA) is a common global public health problem as it contributes to 13% of intra-abdominal abscesses [1]. With advancements in diagnostic microbiology, imaging technology, improved understanding of sepsis and critical care, and minimally invasive image-guided interventions such as percutaneous drainage (PD), clinical outcomes continue to improve; however, PLA-related mortality remains high, in the range of 10–30% [2]. Patient factors, disease factors, and treatment-related factors determine the clinical outcomes of PLA. Patient factors include underlying hypertension, diabetes mellitus (DM), Eastern Cooperative Oncology Group (ECOG) performance status, and Acute Physiology and Chronic Health Evaluation (APACHE) II score [3][4][5]. Disease factors include size, number of abscesses, and presence of gas formation [6][7]. Treatment-related factors include policies for PD, adoption of a liver abscess care bundle, and compliance with the sepsis bundle with local antimicrobial stewardship initiatives [8][9].

Microbiology of PLA has also been shown to impact outcomes in PLA [8]. *Klebsiella pneumoniae* (KP) is the leading causative organism for PLA, followed by *Escherichia coli* (EC) [2][10][11]. *Klebsiella pneumoniae* pyogenic liver abscess (KPPLA) is associated with DM and gas formation, possibly impacting clinical outcomes [7][12]. Some studies have also reported that KPPLA is associated with solitary abscess allowing for easier PD [13], but this has been refuted by others [14]. Serious metastatic complications secondary to haematogenous seeding (e.g., endogenous endophthalmitis) have also been reported with non-hypervirulent and hypervirulent strains, with a reported incidence of 3–11% [15]. ECPLA is more common in older patients and patients with underlying cardiac co-morbidity and biliary disease, and has been associated with small and multiple abscesses, which could impact clinical outcomes [8][16]. PLA due to other aetiologic organisms are uncommon and are not widely compared with KPPLA. To date, there are isolated reports of outcomes of KPPLA or non-KPPLA (N-KPPLA) from various institutes.

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KP is the most common pathogen widely and increasingly implicated in the causation of PLA [17]. Due to the unique peculiarities of KP, it is possible that clinical outcomes of PLA could differ based on microbial aetiology. For example, KPPLA is associated with metastatic complications, coined as KP invasive liver abscess syndrome (KPIS). KPIS was first reported in the 1980s in Southeast Asia [18]. Researchers' study validates this finding, with overall higher metastatic complications in KPPLA than N-KPPLA (OR 2.95, 95% CI: 1.80, 4.84, *p* < 0.001). This phenomenon has been attributed to the unique virulent characteristics of KP (coined as hypervirulent KP (hvKP)), which includes hypermucoviscosity phenotype in K1 and K2 capsular serotypes, mucoviscosity-associated gene A (magA), and regulator of mucoid phenotype A (rmpA) [19]. Wang et al. showed a high prevalence of hvKP (89.1%) in their study on 131 KP isolates, with increased expression of rmpA and aerobactin [20]. Aerobactin allows KP to compete for iron sources in the host and plays

an important role in the virulence of KP [21]. Endophthalmitis, one of the metastatic complications of KPPLA, has also been reported to be increasingly prevalent as a cause of endogenous endophthalmitis in Asia, ranging from 54–61% [15][22][23]. While researchers' meta-analysis failed to demonstrate a significant difference in endophthalmitis between KPPLA and N-KPPLA (OR 2.80, 95% CI: 0.84, 9.34, p = 0.09), this is likely attributed to the small number of studies (n = 5) and low incidence of endophthalmitis (KPPLA n = 20/1162 (1.7%) vs. N-KPPLA n = 1/297 (0.3%)). Similarly, researchers failed to show higher incidence of brain abscess or meningitis in KPPLA; but caution should be taken to interpret these results due to the low sample size and positive cases reported.

DM has been reported to be a risk factor for KPPLA [24][25]. Researchers' meta-analysis similarly demonstrated a higher incidence of DM in patients with KPPLA with pooled OR of 2.35. While higher metastatic complications of KPPLA have been attributed to hvKP, it has been postulated that DM is a host susceptibility factor for metastatic complications [26]. Translational research by Lee et al. showed that DM is associated with a slight reduction in Th1 cytokine production in mononuclear cells, which may impact efficient control and clearance of infection [27]. DM also increases the expression of G protein-coupled receptor kinase 2 (GRK2), which phosphorylates serine/threonine residues on CXCR2 (a G protein-coupled receptor expressed on the neutrophil surface) [28], resulting in recycling or degradation of neutrophils [29]. This reduces the rolling, adhesion, and migration of neutrophils to the infection site [30], resulting in impaired clearance of infection and may explain the higher incidence of metastatic complications in KPPLA.

Researchers' study also demonstrated lower mortality in KPPLA compared to N-KPPLA. This finding was similarly described in narrative reviews and various studies [31][32][33][34]. There are several factors which researchers need to consider. Firstly, baseline demographics and illness severity may predispose N-KPPLA to worse outcomes. For instance, Chen et al. in 2007, who studied 202 patients, showed higher, but not statistically significant mortality in ECPLA compared to KPPLA (26% vs. 4%, adjusted OR 4.2, p = 0.105) [16]. Multivariate analysis on predictors of mortality in ECPLA showed that Acute Physiology and Chronic Health Evaluation (APACHE) II score and underlying malignancy were predictors of mortality (adjusted OR 1.7, 95% CI: 1.1–2.6, p = 0.021, and adjusted OR 26 (95% CI: 1.8–370, p = 0.016), respectively) [16]. None of the individual studies showed significantly lower mortality in KPPLA than N-KPPLA. However, overall mortality across all studies is about half in KPPLA compared to N-KPPLA (KPPLA: 3.9% vs. N-KPPLA 7.6%). Pooled OR in researchers' meta-analysis also showed significantly lower mortality (OR 0.51, 95% CI: 0.34, 0.78, p < 0.001). Repetitive testing of significance by pooling of results in the meta-analysis may have resulted in the rejection of null hypothesis and type 1 error (i.e., demonstrating that there is statistically significant lower mortality in KPPLA even though the results may not be significant). Therefore, cumulative analysis and TSA was performed to control for random errors. Both methods showed that no further studies are required to demonstrate lower mortality in KPPLA, and the rejection of the null hypothesis is not by chance. However, it cannot be determined if the lower mortality is due to fewer co-morbidities, disease attributes, or due to differences in virulent factors.

Interestingly, while it was shown that overall metastatic complications are higher in KPPLA, KPPLA is associated with lower mortality. Plausible explanations for higher overall metastatic complications have been described above: virulence factors and host factors (i.e., DM causing impaired immune function). Impaired immune function secondary to DM has resulted in higher mortality [30]. This was not observed in researchers' study. The management of sepsis, particularly PLA involves a multi-modal approach with an interdisciplinary team involving surgeons, interventional radiologists, infectious disease physicians, and nurses [8]. Apart from treatment with antibiotics, source control is crucial [35]. Researchers showed that KPPLA is associated with solitary and unilobar abscesses, which are more easily drained. This is reinforced by researchers' findings that more KPPLA were likely to undergo PD (p = 0.01) and had a trend towards lower incidence of SD (p = 0.11), though this did not reach statistical significance. SD is usually reserved for PLA refractory to less invasive therapy (i.e., antibiotics, percutaneous aspiration, and/or drainage) [9]. Researchers also found that KPPLA is associated with multi-loculation. Some series have shown that multi-loculation results in the compartmentalization of abscesses and may lead to poor drainage, requiring the need for SD for a breakdown of loculations [36][37]. Multivariate analysis by Haider et al. demonstrated that the presence of multiple abscesses is independently associated with primary failure of PD, but not multi-loculation [38]. This may explain why despite the association of KPPLA with multi-loculation, there is adequate drainage with lower mortality.

An interesting consideration is that, while researchers showed KPPLA has lower mortality compared to N-KPPLA, KP is not associated with lower mortality in other pathologies. For instance, Chan et al. demonstrated that KP bacteremia is associated with higher 30-day mortality (OR 6.09, 95% CI: 1.27–29.10, p = 0.025) compared to *Escherichia coli* in acute cholangitis [39]. They postulated that higher mortality in KP bacteremia might be due to virulence factors and higher antibiotic resistance in KP [40]. A plausible explanation for the difference in findings between pathologies with the same organism, i.e., KP, may be due to demographic and radiological differences. For instance, KPPLA is more common in younger patients and in patients without underlying hepatobiliary disease or malignancy. Malignancy is a known predictor

of poor prognosis in several infections; haematological malignancies result in dysfunctional white blood cells, which reduces immunological function. Patients may also be on cytotoxic chemotherapy for solid organ malignancies, resulting in an immunocompromised state [41][42]. PLA of biliary origin has also been shown to be independently associated with mortality [43]. Underlying hepatobiliary diseases may result in co-existing biliary tract infections, resulting in worse outcomes [16]. While DM results in an immunocompromised state resulting in an increased risk of infections [44], it is also more often associated with cryptogenic PLA, younger patients, and better outcomes [16]. As mentioned above, there is increasing antibiotic resistance in KP. A recent study on 370 isolates of KP showed detection of NDM-1, OXA-48, and ESBL (TEM, SHV, and CTX-M) in two K2 serotypes of KP [45]. While researchers' current results show lower mortality in KPPLA, this may change in the future with multi-drug resistant strains.

Gas formation is an important radiological finding in PLA. Reports have associated the presence of gas formation, i.e., gas-forming PLA (GFPLA) with KP and higher mortality [7][46][47]. A more recent study in 2020, however showed similar mortality and incidence of KP between GFPLA and non-GFPLA [48]. Researchers' meta-analysis failed to demonstrate significant differences in GFPLA between KPPLA and N-KPPLA (OR 1.04, 95% CI: 0.59, 1.83, p = 0.90). Gas formation is an imaging biomarker that is due to the fermentation of mixed acid within the abscess by formic hydrogenlyase, an enzyme produced by certain bacteria [49]. A narrative review in 2018 by Thng et al. on GFPLA showed that KP was more common in GFPLA compared to non-GFPLA in various studies; for instance, Chou et al. studied 424 patients and showed 87.0% of patients with KPPLA had gas formation compared to 63.2% without gas formation [50]. However, researchers' study cannot confirm the clinical outcomes between GFPLA and non-GFPLA.

Researchers' study has its strengths. Researchers obtained a large overall sample size with 16 included articles and 5127 patients. Researchers' study also utilized cumulative analysis and TSA to control for random error and concluded that no further studies are required to investigate mortality differences between KPPLA and N-KPPLA. However, researchers' study also has limitations. Firstly, non-KP bacteria were grouped as "N-KPPLA". No subgroup analysis was performed for mortality in patients with metastatic complications versus no metastatic complications due to the low number of studies reporting these outcomes. Researchers also did not analyze the virulence of KPPLA and non-KPPLA in the study (e.g., whether worse outcomes are due to K1 or K2 capsular serotypes) as these were not included in the studies which compared outcomes of KPPLA versus non-KPPLA apart from one study [20]. This also highlights the lack of reporting on microbiology details alongside clinical outcomes and vice versa, and calls for multidisciplinary collaboration. KPPLA has also been associated with the risk of subsequent colorectal cancer; however, this was only reported in one study, and hence Researchers were unable to perform a quantitative analysis on the risk of colorectal cancer [51]. While researchers collected data on underlying hepatobiliary diseases and history of malignancy, the majority of included studies did not specify the details, e.g., type of malignancy (hematological vs. solid organ) or whether the patient is on chemotherapy, and these may confound outcomes. Lastly, the impact of local resource constraints, compliance to sepsis bundle, implementation of antibiotic stewardship initiatives, and lack of antibiotic resistance data limits the generalizability of researchers' results.

References

1. Altemeier, W.; Culbertson, W.; Fullen, W.; Shook, C.D. Intra-abdominal abscesses. Am. J. Surg. 1973, 125, 70–79.

2. Huang, C.-J.; Pitt, H.A.; Lipsett, P.A.; Osterman, F.A.J.; Lillemoe, K.D.; Cameron, J.L.; Zuidema, G.D. Pyogenic hepatic abscess: Changing trends over 42 years. Ann. Surg. 1996, 223, 600–609.

3. Lo, J.Z.W.; Leow, J.J.J.; Ng, P.L.F.; Lee, H.Q.; Mohd Noor, N.A.; Low, J.K.; Junnarkar, S.P.; Woon, W.W.L. Predictors of therapy failure in a series of 741 adult pyogenic liver abscesses. J. Hepato-Biliary-Pancreat. Sci. 2015, 22, 156–165.

4. Hope, W.W.; Vrochides, D.V.; Newcomb, W.L.; Mayo-Smith, W.W.; Iannitti, D.A. Optimal treatment of hepatic abscess. Am. Surg. 2008, 74, 178–182.

5. Hsieh, H.F.; Chen, T.W.; Yu, C.Y.; Wang, N.C.; Chu, H.C.; Shih, M.L.; Yu, J.C.; Hsieh, C.B. Aggressive hepatic resection for patients with pyogenic liver abscess and APACHE II score ≥ 15. Am. J. Surg. 2008, 196, 346–350.

6. Liao, W.I.; Tsai, S.-H.; Yu, C.Y.; Huang, G.S.; Lin, Y.Y.; Hsu, C.W.; Hsu, H.H.; Chang, W.C. Pyogenic liver abscess treated by percutaneous catheter drainage: MDCT measurement for treatment outcome. Eur. J. Radiol. 2012, 81, 609–615.

7. Thng, C.B.; Tan, Y.P.; Shelat, V.G. Gas-forming pyogenic liver abscess: A world review. Ann. Hepatobiliary Pancreat Surg. 2018, 22, 11–18.

8. Shelat, V.G.; Chia, C.L.K.; Yeo, C.S.W.; Qiao, W.; Woon, W.; Junnarkar, S.P. Pyogenic Liver Abscess: Does Escherichia Coli Cause more Adverse Outcomes than Klebsiella Pneumoniae? World J. Surg. 2015, 39, 2535–2542.

9. Chan, K.S.; Shelat, V. Pyogenic Liver Abscess. In The IASGO Textbook of Multi-Disciplinary Management of Hepato-Pancreato-Biliary Diseases; Makuuchi, M., Kokudo, N., Popescu, I., Belghiti, J., Han, H.S., Takaori, K., Duda, D.G., Eds.; Springer Nature Singapore: Singapore, 2022; pp. 509–519.

10. Branum, G.D.; Tyson, G.S.; Branum, M.A.; Meyers, W.C. Hepatic abscess. Changes in etiology, diagnosis, and management. Ann. Surg. 1990, 212, 655.

11. Rahimian, J.; Wilson, T.; Oram, V.; Holzman, R.S. Pyogenic liver abscess: Recent trends in etiology and mortality. Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 2004, 39, 1654–1659.

12. Lin, Y.T.; Wang, F.D.; Wu, P.F.; Fung, C.P. Klebsiella pneumoniae liver abscess in diabetic patients: Association of glycemic control with the clinical characteristics. BMC Infect. Dis. 2013, 13, 56.

13. Alsaif, H.S.; Venkatesh, S.K.; Chan, D.S.; Archuleta, S. CT appearance of pyogenic liver abscesses caused by Klebsiella pneumoniae. Radiology 2011, 260, 129–138.

14. Yin, D.; Ji, C.; Zhang, S.; Wang, J.; Lu, Z.; Song, X.; Jiang, H.; Lau, W.Y.; Liu, L. Clinical characteristics and management of 1572 patients with pyogenic liver abscess: A 12-year retrospective study. Liver Int. 2021, 41, 810–818.

15. Sheu, S.J.; Kung, Y.H.; Wu, T.T.; Chang, F.P.; Horng, Y.H. Risk factors for endogenous endophthalmitis secondary to klebsiella pneumoniae liver abscess: 20-year experience in Southern Taiwan. Retina 2011, 31, 2026–2031.

16. Chen, S.C.; Wu, W.Y.; Yeh, C.H.; Lai, K.C.; Cheng, K.S.; Jeng, L.B.; Wang, P.H.; Lin, D.B.; Chen, C.C.; Lee, M.C.; et al. Comparison of Escherichia coli and Klebsiella pneumoniae liver abscesses. Am. J. Med. Sci. 2007, 334, 97–105.

17. Lee, B.J.; Sim, K.; Shelat, V.G. Pyogenic liver abscess. Taylor's Recent Adv. Surg. 2018, 39, 113–124.

18. Liu, Y.C.; Cheng, D.L.; Lin, C.L. Klebsiella pneumoniae liver abscess associated with septic endophthalmitis. Arch. Intern. Med. 1986, 146, 1913–1916.

19. Siu, L.K.; Yeh, K.M.; Lin, J.C.; Fung, C.P.; Chang, F.Y. Klebsiella pneumoniae liver abscess: A new invasive syndrome. Lancet Infect. Dis. 2012, 12, 881–887.

20. Wang, J.; Yan, Y.; Xue, X.; Wang, K.; Shen, D. Comparison of pyogenic liver abscesses caused by hypermucoviscous Klebsiella pneumoniae and non-Klebsiella pneumoniae pathogens in Beijing: A retrospective analysis. J. Int. Med. Res. 2013, 41, 1088–1097.

21. Wu, M.C.; Lin, T.L.; Hsieh, P.F.; Yang, H.C.; Wang, J.T. Isolation of genes involved in biofilm formation of a Klebsiella pneumoniae strain causing pyogenic liver abscess. PLoS ONE 2011, 6, e23500.

22. Wong, J.S.; Chan, T.K.; Lee, H.M.; Chee, S.P. Endogenous bacterial endophthalmitis: An east Asian experience and a reappraisal of a severe ocular affliction. Ophthalmology 2000, 107, 1483–1491.

23. Chen, Y.J.; Kuo, H.K.; Wu, P.C.; Kuo, M.L.; Tsai, H.H.; Liu, C.C.; Chen, C.H. A 10-year comparison of endogenous endophthalmitis outcomes: An east Asian experience with Klebsiella pneumoniae infection. Retina 2004, 24, 383–390.

24. Lee, I.R.; Molton, J.S.; Wyres, K.L.; Gorrie, C.; Wong, J.; Hoh, C.H.; Teo, J.; Kalimuddin, S.; Lye, D.C.; Archuleta, S.; et al. Differential host susceptibility and bacterial virulence factors driving Klebsiella liver abscess in an ethnically diverse population. Sci. Rep. 2016, 6, 29316.

25. Fang, C.T.; Lai, S.Y.; Yi, W.C.; Hsueh, P.R.; Liu, K.L.; Chang, S.C. Klebsiella pneumoniae genotype K1: An emerging pathogen that causes septic ocular or central nervous system complications from pyogenic liver abscess. Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 2007, 45, 284–293.

26. Fung, C.P.; Chang, F.Y.; Lee, S.C.; Hu, B.S.; Kuo, B.I.; Liu, C.Y.; Ho, M.; Siu, L.K. A global emerging disease of Klebsiella pneumoniae liver abscess: Is serotype K1 an important factor for complicated endophthalmitis? Gut 2002, 50, 420–424.

27. Lee, I.R.; Sng, E.; Lee, K.O.; Molton, J.S.; Chan, M.; Kalimuddin, S.; Izharuddin, E.; Lye, D.C.; Archuleta, S.; Gan, Y.H. Comparison of Diabetic and Non-diabetic Human Leukocytic Responses to Different Capsule Types of Klebsiella pneumoniae Responsible for Causing Pyogenic Liver Abscess. Front. Cell Infect. Microbiol. 2017, 7, 401.

28. Spiller, F.; Carlos, D.; Souto, F.O.; de Freitas, A.; Soares, F.S.; Vieira, S.M.; Paula, F.J.; Alves-Filho, J.C.; Cunha, F.Q. α1-Acid glycoprotein decreases neutrophil migration and increases susceptibility to sepsis in diabetic mice. Diabetes 2012, 61, 1584–1591.

29. Rios-Santos, F.; Alves-Filho, J.C.; Souto, F.O.; Spiller, F.; Freitas, A.; Lotufo, C.M.; Soares, M.B.; Dos Santos, R.R.; Teixeira, M.M.; Cunha, F.Q. Down-regulation of CXCR2 on neutrophils in severe sepsis is mediated by inducible nitric oxide synthase-derived nitric oxide. Am. J. Respir. Crit. Care Med. 2007, 175, 490–497.

30. Trevelin, S.C.; Carlos, D.; Beretta, M.; da Silva, J.S.; Cunha, F.Q. Diabetes Mellitus and Sepsis: A Challenging Association. Shock 2017, 47, 276–287.

31. Liu, Y.; Wang, J.Y.; Jiang, W. An Increasing Prominent Disease of Klebsiella pneumoniae Liver Abscess: Etiology, Diagnosis, and Treatment. Gastroenterol. Res. Pr. 2013, 2013, 258514.

32. Wang, J.H.; Liu, Y.C.; Lee, S.S.; Yen, M.Y.; Chen, Y.S.; Wang, J.H.; Wann, S.R.; Lin, H.H. Primary liver abscess due to Klebsiella pneumoniae in Taiwan. Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 1998, 26, 1434–1438.

33. Tsai, F.C.; Huang, Y.T.; Chang, L.Y.; Wang, J.T. Pyogenic liver abscess as endemic disease, Taiwan. Emerg. Infect. Dis. 2008, 14, 1592–1600.

34. Yang, C.-C.; Yen, C.-H.; Ho, M.-W.; Wang, J.-H. Comparison of pyogenic liver abscess caused by non-Klebsiella pneumoniae and Klebsiella pneumoniae. J. Microbiol. Immunol. Infect. 2004, 37, 176–184.

35. Dellinger, R.P.; Levy, M.M.; Rhodes, A.; Annane, D.; Gerlach, H.; Opal, S.M.; Sevransky, J.E.; Sprung, C.L.; Douglas, I.S.; Jaeschke, R. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013, 39, 165–228.

36. Farges, O.; Leese, T.; Bismuth, H. Pyogenic liver abscess: An improvement in prognosis. Br. J. Surg. 1988, 75, 862–865.

37. Barakate, M.S.; Stephen, M.S.; Waugh, R.C.; Gallagher, P.J.; Solomon, M.J.; Storey, D.W.; Sheldon, D.M. Pyogenic Liver Abscess: A review of 10 years' experience in management. Aust. N. Zealand J. Surg. 1999, 69, 205–209.

38. Haider, S.J.; Tarulli, M.; McNulty, N.J.; Hoffer, E.K. Liver Abscesses: Factors That Influence Outcome of Percutaneous Drainage. AJR Am. J. Roentgenol. 2017, 209, 205–213.

39. Chan, K.S.; Shelat, V.G. Klebsiella pneumoniae Bacteremia is Associated with Higher Mortality in Acute Calculous Cholangitis as Compared to Escherichia coli Bacteremia. World J. Surg. 2022, 46, 1678–1685.

40. Hsu, L.-Y.; Tan, T.-Y.; Jureen, R.; Koh, T.-H.; Krishnan, P.; Tzer-Pin Lin, R.; Wen-Sin Tee, N.; Tambyah, P.A. Antimicrobial drug resistance in Singapore hospitals. Emerg Infect. Dis. 2007, 13, 1944–1947.

41. Lainey, E.; Wolfromm, A.; Sukkurwala, A.Q.; Micol, J.B.; Fenaux, P.; Galluzzi, L.; Kepp, O.; Kroemer, G. EGFR inhibitors exacerbate differentiation and cell cycle arrest induced by retinoic acid and vitamin D3 in acute myeloid leukemia cells. Cell Cycle 2013, 12, 2978–2991.

42. Albiges, L.; Foulon, S.; Bayle, A.; Gachot, B.; Pommeret, F.; Willekens, C.; Stoclin, A.; Merad, M.; Griscelli, F.; Lacroix, L.; et al. Determinants of the outcomes of patients with cancer infected with SARS-CoV-2: Results from the Gustave Roussy cohort. Nat. Cancer 2020, 1, 965–975.

43. Alvarez Pérez, J.A.; González, J.J.; Baldonedo, R.F.; Sanz, L.; Carreño, G.; Junco, A.; Rodríguez, J.I.; Martínez, M.a. D.; Jorge, J.I. Clinical course, treatment, and multivariate analysis of risk factors for pyogenic liver abscess. Am. J. Surg. 2001, 181, 177–186.

44. Akash, M.S.H.; Rehman, K.; Fiayyaz, F.; Sabir, S.; Khurshid, M. Diabetes-associated infections: Development of antimicrobial resistance and possible treatment strategies. Arch. Microbiol. 2020, 202, 953–965.

45. Remya, P.; Shanthi, M.; Sekar, U. Occurrence and characterization of hyperviscous K1 and K2 serotype in Klebsiella pneumoniae. J. Lab. Physicians 2018, 10, 283–288.

46. Yang, C.-C.; Chen, C.-Y.; Lin, X.-Z.; Chang, T.-T.; Shin, J.-S.; Lin, C.-Y. Pyogenic liver abscess in Taiwan: Emphasis on gas-forming liver abscess in diabetics. Am. J. Gastroenterol. 1993, 88, 1911–1915.

47. Lee, T.-Y.; Wan, Y.-L.; Tsai, C.-C. Gas-containing liver abscess: Radiological findings and clinical significance. Abdom. Imaging 1994, 19, 47–52.

48. Chan, K.S.; Thng, C.B.; Chan, Y.-H.; Shelat, V.G. Outcomes of Gas-Forming Pyogenic Liver Abscess Are Comparable to Non-Gas-Forming Pyogenic Liver Abscess in the Era of Multi-Modal Care: A Propensity Score Matched Study. Surg. Infect. 2020, 21, 884–890.

49. Chong, V.; Yong, A.; Wahab, A. Gas-forming pyogenic liver abscess. Singap. Med. J. 2008, 49, e123–e125.

50. Chou, F.F.; Sheen-Chen, S.M.; Chen, Y.S.; Lee, T.Y. The comparison of clinical course and results of treatment between gas-forming and non-gas-forming pyogenic liver abscess. Arch. Surg. 1995, 130, 401–405.

51. Huang, W.K.; Chang, J.C.; See, L.C.; Tu, H.T.; Chen, J.S.; Liaw, C.C.; Lin, Y.C.; Yang, T.S. Higher rate of colorectal cancer among patients with pyogenic liver abscess with Klebsiella pneumoniae than those without: An 11-year follow-up study. Colorectal Dis. 2012, 14, e794–e801.