INTERNATIONAL JOURNAL OF HEALTH & MEDICAL RESEARCH

ISSN(print): 2833-213X, ISSN(online): 2833-2148

Volume 03 Issue 09 September 2024

DOI : 10.58806/ijhmr.2024.v3i09n04

Page No. 670-674

Pathogenic Bacteria Associated with Cholecystitis: A Review Article

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ABSTRACT: Cholecystitis is defined as an inflammation of the gallbladder. It is of major concern because if left untreated, it can progress to complex pathologies. The high burden of cholecystitis underlines the importance of epidemiological knowledge regarding its prevalence, risk factors, and related comorbid conditions for proper planning of preventive and therapeutic measures. This literature review presents recent insights into the bacteria causing cholecystitis, the problem of multidrug resistance, and the hypothetical effect of the gut microbiome on the health of the gallbladder.

1. INTRODUCTION

Cholecystitis, an inflammation of the gallbladder, is of major health concern and can be a source of otherwise avoidable life-threatening complications. Knowledge of the epidemiology of cholecystitis with respect to prevalence, risk factors, and comorbidities is essential for practical prevention and treatment measures. Cholecystitis is generally connected with infections and most often bacterial. Knowledge of the associated microbial community is important for an accurate diagnosis of the patient and proper choice of a treatment method. The current review compiles up-to-date information on bacterial etiology in cholecystitis, importance related to multi-drug resistant organisms, and potential impact of gut microbiota on health status of the gallbladder. It also comprises a contemporary perspective on the existing understanding in the field of epidemiology of cholecystitis, areas where knowledge is lacking, and some potential directions for future study.

PREVALENCE AND INCIDENCE

Cholecystitis is a proxy for the burden of gallbladder diseases, which results from a complex interaction of varying population-attributable risk factors. Though information on cholecystitis specifically is lacking in the literature, information on estimated related gastrointestinal problems can be adduced or pooled together. For example, Younossi et al. pointed out in 2018 that non-alcoholic fatty liver disease is rising, leading to an increase in the burden of cholecystitis, since it shares common risk factors with the latter—for instance, obesity, and metabolic syndrome. This would indicate a rise in cholecystitis cases, meaning that the gallbladder diseases' epidemiology should be monitored simultaneously with liver conditions. (Younossi et al., 2018).

RISK FACTORS

Research has identified several risk factors that play a role in the development of cholecystitis. Ananthakrishnan (2015) has emphasized that inflammatory bowel disease has a role in the alteration of the function of the gallbladder, especially when it is at risk for cholecystitis. In this condition, the composition of bile is likely to be impaired and the motility of the gallbladder may increase the form of stones that will eventually lead to cholecystitis (Ananthakrishnan, 2015). Obesity is also a significant risk factor for cholecystitis because it is closely related to NAFLD-related hepatocellular carcinoma. This usually leads to irritation due to saturation disordering the bile of cholesterol in a way that increases the level of its saturation (Huang et al., 2020).

COMORBIDITIES

The connection of cholecystitis to comorbidity has been highlighted in recent research. For example, in their work, Leon and Maddox (2015) discuss how diabetes interacts with cardiovascular disease, which also might apply to the health of the gallbladder. Diabetes is associated with abnormal gallbladder motility and an increased risk for the formation of gallstones—factors that could precipitate cholecystitis (Leon & Maddox, 2015).

Moreover, the contribution of diet and lifestyle factors such as a high-fat diet and inactivity in the pathogenesis of gallbladder diseases, including cholecystitis, cannot be diminished. These factors add to obesity and metabolic syndrome, both acting as independent risk factors for gallbladder inflammation.

BACTERIAL COMMUNITIES IN CHOLECYSTITIS

Research indicates the bacteria related to cholecystitis are of wide diversity, mainly Gram-negative organisms. In particular, studies have emphasized Escherichia coli and Klebsiella pneumoniae to be major pathogenic agents causing the infection. These bacteria are responsible not only for acute cholecystitis but also for the vast majority of cases of recurrent infection, which represents a serious problem for the management of the patient (Magiorakos et al., 2012).

The gut microbiota composition is of prime significance for general health conditions and disease, including gastrointestinal infections. According to the study conducted by Lynch & Pedersen (2016), one of the key roles is assigned to the balanced microbiota in holding back the overgrowth of pathogenic bacteria; that could be a cause of cholecystitis. The other way an imbalance in the microbiome may contribute to infection is by promoting the establishment of infectious bacteria due to improper treatment.

Moreover, gut microbiome studies have unveiled changes associated with systemic disease, implying an influence on conditions such as cholecystitis. For example, in their study, Franciosa et al. (2018) stated that dysbiosis can cause inflammatory reactions hence complicating events and diseases to cholecystitis. This brings out the importance of more research into the relationship between the gut-liver axis and diseases of the gallbladder.

Bacteria have been associated as a key player in the pathology of cholecystitis and E. coli tops the list. It has been revealed that, in acute cases of cholecystitis, E. coli is the most frequently isolated organism and accounts for about 29% of isolates (Johnson et al., 2019). The incidence acts to drive home the fact of its role in the processes of infection leading to gallbladder inflammation. Some strains of E. coli, among them adherent invasive E. coli (AIEC), have been described as able to adhere to and invade epithelial intestinal cells (Mitchell et al., 2019; Liu et al., 2020). This contributes not only to the local initiation of processes that favor its own persistence—such as inflammation but also could make conditions like cholecystitis more severe. Interaction between AIEC and the intestinal mucosa might initiate the inflammatory response or aggravate it in patients already known to have a risk of gallbladder diseases.

Moreover, the competitive interactions of E. coli with other gut microbiota could influence human gut health in general, and thus, possibly the incidence of cholecystitis. Microbial composition and their functional profiles are dynamic and can be influenced by several factors, including diet, antibiotics, and host immune responses (Dhariwal et al., 2017; Chong et al., 2020). These changes in microbiota could influence the virulence properties of E. coli and therefore its involvement in cholecystitis.

Iron acquisition is a key determinant enabling E. coli to survive and exhibit virulence within a host (Skaar, 2010). Fe (III) is sequestered by the host during the inflammatory process to limit bacterial replication, but E. coli has evolved ways to bypass this limitation, thereby enhancing its pathogenic potential. The cross-talk of E. coli iron uptake systems with those of the host immune response machinery is still an enigma and represents a valuable area for study to determine how such interactions influence the progression of cholecystitis.

RESISTANCE PATTERNS AND CLINICAL IMPLICATIONS

Indeed, the emergence of multidrug-resistant bacteria poses a considerable challenge in the treatment of cholecystitis. As Tacconelli et al. (2014) note, with the prevalence of multidrug-resistant Gram-negative bacteria in healthcare settings, stringent infection measures become necessary to avert transmission. The very existence of these strains in turn compels a variety of treatment options which often results in prolonged hospital stays for an individual and increased morbidity.

In addition to this, emerging reports, including the study by Tamma et al. (2021), document the management of ESBL-producing Enterobacterales, which predominantly cause the increasingly identified infections noted in cholecystitis. With growing emergent reports, robust clinical guidelines that address the control of these resistant infections become a dire need, standard therapies rendered possibly ineffective for their elimination.

CONCLUSION

In summary, though there is a well-established literature body that deals with the epidemiology of related gastrointestinal conditions, specific research related to cholecystitis is limited. By filling in the gaps of knowledge described in this review's future directions for research and pursuing them, the healthcare community can better understand cholecystitis and, in the end, more effective prevention and treatment strategies will be developed. The bacteria connected with cholecystitis, especially strains that are multidrug resistant, are a considerable challenge to management that is effective. Therefore, it is important to understand the interaction of the gut microbiome with gallbladder health in order to create comprehensive treatment approaches. Answering these identified knowledge gaps through specially targeted research would increase our understanding of cholecystitis and improve clinical outcomes for patients.

REFERENCES

1) Ahmadi, B.., Alimohammadian, Masoomeh., Yaseri, M.., Majidi, A.., Boreiri, Majid., Islami, F.., Poustchi, H.., Derakhshan, M.., Feizesani, Akabar., Pourshams, A.., Abnet, C.., Brennan, Paul., Dawsey, S.., Kamangar, F.., Boffetta, P.., Sadjadi, A.., & Malekzadeh, R.. (2016). Multimorbidity: Epidemiology and Risk Factors in the Golestan Cohort Study, Iran. Medicine , 95 . http://doi.org/10.1097/MD.0000000000002756
2) Ananthakrishnan, A.. (2015). Epidemiology and risk factors for IBD. *Nature Reviews Gastroenterology &Hepatology* , 12 , 205-217 . http://doi.org/10.1038/nrgastro.2015.34
3) Chong, Jasmine., Liu, Peng., Zhou, Guangyan., & Xia, J.. (2020). Using MicrobiomeAnalyst for comprehensive statistical, functional, and meta-analysis of microbiome data. *Nature Protocols* , 15 , 799 - 821 . http://doi.org/10.1038/s41596-019-0264-1
4) Clemente, J.., Manasson, J.., & Scher, J.. (2018). The role of the gut microbiome in systemic inflammatory disease. *British Medical Journal* , 360 . http://doi.org/10.1136/bmj.j5145
5) Dehlin, M.., Jacobsson, L.., & Roddy, E.. (2020). Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nature Reviews Rheumatology* , 16 , 380-390 . http://doi.org/10.1038/s41584-020-0441-1
6) Dhariwal, A.., Chong, Jasmine., Habib, Salam., King, Irah L.., Agellon, L.., & Xia, J.. (2017). MicrobiomeAnalyst: a web-based tool for comprehensive statistical, visual and meta-analysis of microbiome data. *Nucleic Acids Research* , 45 , W180 - W188 . http://doi.org/10.1093/nar/gkx295
7) Exner, M.., Bhattacharya, S.., Christiansen, B.., Gebel, J.., Goroncy-Bermes, P.., Hartemann, P.., Heeg, P.., Ilschner, C.., Kramer, A.., Larson, E.., Merkens, W.., Mielke, M.., Oltmanns, P.., Ross, B.., Rotter, M.., Schmithausen, R.., Sonntag, H.., & Trautmann, M.. (2017). Antibiotic resistance: What is so special about multidrug-resistant Gram-negative bacteria?. *GMS Hygiene and Infection Control* , 12 . http://doi.org/10.3205/dgkh000290
8) Franzosa, E.., Sirota-Madi, Alexandra., Ávila-Pacheco, J.., Fornelos, Nadine., Haiser, Henry J.., Reinker, S.., Vatanen, T.., Hall, A. B.., FASA, Himel Mallick, PhD,., McIver, L.., Sauk, J.., Wilson, R.., Stevens, B.., Scott, Justin., Pierce, K.., Deik, A.., Bullock, Kevin., Imhann, F.., Porter, Jeffrey A.., Zhernakova, A.., Fu, Jingyuan., Weersma, R.., Wijmenga, C.., Clish, C.., Vlamakis, H.., Huttenhower, C.., & Xavier, R.. (2018). Gut microbiome structure and metabolic activity in inflammatory bowel disease. *Nature microbiology* , 4 , 293 - 305 . http://doi.org/10.1038/s41564-018-0306-4
9) Freifeld, A.., Bow, E.., Sepkowitz, K.., Boeckh, M.., Ito, J.., Mullen, C.., Raad, I.., Rolston, K.., Young, Jo-Anne H.., & Wingard, J.. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america.. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* , 52 4 , e56-93 . http://doi.org/10.1093/cid/cir073
10) He, Yan., Wu, Wei., Zheng, Huimin., Li, Pan., McDonald, Daniel., Sheng, Hua-fang., Chen, Muxuan., Chen, Zi-hui., Ji, G.., Zheng, Zhong-Dai-Xi., Mujagond, Prabhakar., Chen, Xiao-Jiao., Rong, Zu-hua., Chen, Peng., Lyu, Li-Yi., Wang, Xian., Wu, Chong-Bin., Yu, Nan., Xu, Yanfang., Yin, Jia., Raes, J.., Knight, R.., Ma, W.., & Zhou, Hong-Wei. (2018). Regional variation limits applications of healthy gut microbiome reference ranges and disease models. *Nature Medicine* , 24 , 1532 - 1535 . http://doi.org/10.1038/s41591-018-0164-x
11) Hicks, C.., & Selvin, E.. (2019). Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. *Current Diabetes Reports* , 19 . http://doi.org/10.1007/s11892-019-1212-8
12) Hills, Ronald D., Pontefract, Benjamin A., Mishcon, Hillary R.., Black, C.., Sutton, S. C.., & Theberge, Cory R.. (2019). Gut Microbiome: Profound Implications for Diet and Disease. *Nutrients* , 11 . http://doi.org/10.1159/000523712
13) Holt-Lunstad, J.. (2017). The Potential Public Health Relevance of Social Isolation and Loneliness: Prevalence, Epidemiology, and Risk Factors. *Public Policy & Aging Report* , 27 , 127–130 . http://doi.org/10.1093/ppar/prx030
14) Huang, Daniel Q.., El-Serag, H.., & Loomba, R.. (2020). Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. *Nature Reviews Gastroenterology & Hepatology* , 18 , 223 - 238 . http://doi.org/10.1038/s41575-020-00381-6
15) Jie, Zhuye., Xia, Huihua., Zhong, Shi-long., Feng, Q.., Li, Shenghui., Liang, Suisha., Zhong, Huanzi., Liu, Zhipeng., Gao, Yuan., Zhao, Hui., Zhang, Dongya., Su, Zheng., Fang, Zhiwei., Lan, Zhou., Li, Junhua., Xiao, L.., Li, Jun., Li, Ruijun., Li, Xiaoping., Li, Fei., Ren, Huahui., Huang, Y.., Peng, Yangqing., Li, Guanglei., Wen, Bo., Dong, Bo., Chen, Ji-yan., Geng, Qing-shan., Zhang, Zhiwei., Yang, Huanming., Wang, Jian., Wang, Jun., Zhang, Xuan., Madsen, L.., Brix, S.., Ning, G.., Xu, Xun., Liu, Xin., Hou, Yong., Jia, Huijue., He, K.., & Kristiansen, K.. (2017). The gut microbiome in atherosclerotic cardiovascular disease. *Nature Communications* , 8 . http://doi.org/10.1038/s41467-017-00900-1
16) Johnson, Jethro S.., Spakowicz, Daniel J.., Hong, B.., Petersen, Lauren M.., Demkowicz, Patrick C.., Chen, Lei., Leopold, Shana R.., Hanson, B.., Agresta, Hanako., Gerstein, M.., Sodergren, E.., & Weinstock, G.. (2019). Evaluation of 16S rRNA

gene sequencing for species and strain-level microbiome analysis. *Nature Communications* , 10 . http://doi.org/10.1038/s41467-019-13036-1

17) Kawamoto, Shimpei., Maruya, M.., Kato, Lucia M.., Suda, W.., Atarashi, K.., Doi, Yasuko., Tsutsui, Yumi., Qin, Hongyan., Honda, K.., Okada, T.., Hattori, M.., & Fagarasan, S.. (2014). Foxp3(+) T cells regulate immunoglobulin a selection and facilitate diversification of bacterial species responsible for immune homeostasis.. *Immunity* , 41 1 , 152-65 . http://doi.org/10.1016/j.immuni.2014.05.016
18) Keski-Rahkonen, A.., & Mustelin, L.. (2016). Epidemiology of eating disorders in Europe: prevalence, incidence, comorbidity, course, consequences, and risk factors. *Current Opinion in Psychiatry* , 29 , 340–345 . http://doi.org/10.1097/YCO.0000000000000278
19) Kho, Z. Y.., & Lal, S.. (2018). The Human Gut Microbiome – A Potential Controller of Wellness and Disease. *Frontiers in Microbiology* , 9 . http://doi.org/10.3389/fmicb.2018.01835
20) Klein, A.. (2021). Pancreatic cancer epidemiology: understanding the role of lifestyle and inherited risk factors. *Nature Reviews Gastroenterology & Hepatology* , 18 , 493 - 502 . http://doi.org/10.1038/s41575-021-00457-x
21) Kuo, C.., Grainge, M.., Zhang, Weiya., & Doherty, M.. (2015). Global epidemiology of gout: prevalence, incidence and risk factors. *Nature Reviews Rheumatology* , 11 , 649-662 . http://doi.org/10.1038/nrrheum.2015.91
22) LaSarre, Breah., & Federle, Michael J.. (2013). Exploiting Quorum Sensing To Confuse Bacterial Pathogens. *Microbiology and Molecular Biology Reviews* , 77 , 73 - 111 . http://doi.org/10.1128/MMBR.00046-12
23) Leon, Benjamin., & Maddox, T.. (2015). Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research.. *World journal of diabetes* , 6 13 , 1246-58 . http://doi.org/10.4239/wjd.v6.i13.1246
24) Liu, Yong-xin., Qin, Yuan., Chen, Tong., Lu, Meiping., Qian, Xubo., Guo, Xiaoxuan., & Bai, Yang. (2020). A practical guide to amplicon and metagenomic analysis of microbiome data. *Protein & Cell* , 12 , 315 - 330 . http://doi.org/10.1007/s13238-020-00724-8
25) Lynch, S.., & Pedersen, Oluf. (2016). The Human Intestinal Microbiome in Health and Disease.. *The New England journal of medicine* , 375 24 , 2369-2379 . http://doi.org/10.1056/NEJMRA1600266
26) Magiorakos, A.., Srinivasan, A.., Carey, R.., Carmeli, Y.., Falagas, M.., Falagas, M.., Giske, C.., Harbarth, S.., Hindler, J.., Kahlmeter, G.., Olsson-liljequist, B.., Paterson, D.., Rice, L.., Stelling, J.., Struelens, M.., Vatopoulos, A.., Weber, J.., & Monnet, D.. (2012). Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance.. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* , 18 3 , 268-81 . http://doi.org/10.1111/j.1469-0691.2011.03570.x
27) Manor, Ohad., Dai, C.., Kornilov, S.., Smith, Brett., Price, N.., Lovejoy, J.., Gibbons, S.., & Magis, A.. (2020). Health and disease markers correlate with gut microbiome composition across thousands of people. *Nature Communications* , 11 . http://doi.org/10.1038/s41467-020-18871-1
28) McMurdie, Paul J.., & Holmes, S.. (2013). phyloseq: An R Package for Reproducible Interactive Analysis and Graphics of Microbiome Census Data. *PLoS ONE* , 8 . http://doi.org/10.1371/journal.pone.0061217
29) Mitchell, A.., Almeida, Alexandre., Beracochea, Martin., Boland, M.., Burgin, Josephine., Cochrane, G.., Crusoe, M.., Kale, Varsha., Potter, Simon C.., Richardson, Lorna J.., Sakharova, Ekaterina A.., Scheremetjew, Maxim., Korobeynikov, A.., Shlemov, Alexander., Kunyavskaya, Olga., Lapidus, A.., & Finn, R.. (2019). MGnify: the microbiome analysis resource in 2020. *Nucleic Acids Research* , 48 , D570 - D578 . http://doi.org/10.1093/nar/gkz1035
30) Nutten, S.. (2015). Atopic Dermatitis: Global Epidemiology and Risk Factors. *Annals of Nutrition and Metabolism* , 66 , 8 - 16 . http://doi.org/10.1159/000370220
31) Ramasamy, Dhamodharan., Mishra, A.., Lagier, J.., Padhmanabhan, Roshan., Rossi, Morgane., Sentausa, E.., Raoult, D.., & Fournier, P.. (2014). A polyphasic strategy incorporating genomic data for the taxonomic description of novel bacterial species.. *International journal of systematic and evolutionary microbiology* , 64 Pt 2 , 384-91 . http://doi.org/10.1099/ijs.0.057091-0
32) Ren, Z.., Li, Ang., Jiang, Jianwen., Zhou, Lin., Yu, Zujiang., Lu, Haifeng., Xie, Haiyang., Chen, Xiaolong., Shao, Li., Zhang, Ruiqing., Xu, Shao-Yan., Zhang, Hua., Cui, G.., Chen, Xinhua., Sun, R.., Wen, Hao., Lerut, J.., Kan, Q.., Li, Lanjuan., & Zheng, Shusen. (2018). Gut microbiome analysis as a tool towards targeted non-invasive biomarkers for early hepatocellular carcinoma. *Gut* , 68 , 1014 - 1023 . http://doi.org/10.1136/gutjnl-2017-315084
33) Riviello, E.., Kiviri, W.., Twagirumugabe, T.., Mueller, Ariel., Banner-Goodspeed, V.., Officer, Laurent., Novack, V.., Mutumwinka, M.., Talmor, D.., & Fowler, R.. (2015). Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition.. *American journal of respiratory and critical care medicine* , 193 1 , 52-9 . http://doi.org/10.1164/rccm.201503-0584OC

34) Rodriguez-R, Luis M.., & Konstantinidis, K.. (2014). Bypassing Cultivation To Identify Bacterial Species: Culture-independent genomic approaches identify credibly distinct clusters, avoid cultivation bias, and provide true insights into microbial species. *Microbe Magazine* , 9 , 111-118 . http://doi.org/10.1128/MICROBE.9.111.1
35) Romano, S.., Savva, G.., Bedarf, J.., Charles, I.., Hildebrand, F.., & Narbad, A.. (2021). Meta-analysis of the Parkinson's disease gut microbiome suggests alterations linked to intestinal inflammation. *NPJ Parkinson's Disease* , 7 . http://doi.org/10.1038/s41531-021-00156-z
36) Schirmer, M.., Franzosa, E.., Lloyd-Price, J.., McIver, L.., Schwager, Randall., Poon, Tiffany W.., Ananthakrishnan, A.., Andrews, E.., Barron, G.., Lake, K.., Prasad, M.., Sauk, J.., Stevens, B.., Wilson, R.., Braun, J.., Denson, L.., Kugathasan, S.., McGovern, D.., Vlamakis, H.., Xavier, R.., & Huttenhower, C.. (2018). Dynamics of metatranscription in the inflammatory bowel disease gut microbiome. *Nature microbiology* , 3 , 337 - 346 . http://doi.org/10.1038/s41564-017-0089-z
37) Skaar, Eric P.. (2010). The Battle for Iron between Bacterial Pathogens and Their Vertebrate Hosts. *PLoS Pathogens* , 6 . http://doi.org/10.1371/journal.ppat.1000949
38) Stoll, B.., Hansen, N.., Sánchez, P.., Faix, R.., Poindexter, B.., Meurs, K. V. van., Bizzarro, M.., Goldberg, R.., Frantz, I.., Hale, E.., Shankaran, S.., Kennedy, K.., Carlo, W.., Watterberg, K.., Bell, E.., Walsh, M.., Schibler, K.., Laptook, A.., Shane, A.., Schrag, S.., Das, A.., & Higgins, R.. (2011). Early Onset Neonatal Sepsis: The Burden of Group B Streptococcal and E. coli Disease Continues. *Pediatrics* , 127 , 817 - 826 . http://doi.org/10.1542/peds.2010-2217
39) Tacconelli, E.., Cataldo, M. A.., Dancer, S.., Angelis, G. D.., Falcone, M.., Frank, U.., Kahlmeter, G.., Pan, A.., Petrosillo, N.., Rodríguez-Baño, J.., Rodríguez-Baño, J.., Singh, N.., Venditti, M.., Yokoe, D.., & Cookson, B.. (2014). ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients.. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* , 20 Suppl 1 , 1-55 . http://doi.org/10.1111/1469-0691.12427
40) Tamma, P.., Aitken, S.., Bonomo, R.., Mathers, A.., Duin, D. van., & Clancy, C.. (2021). Infectious Diseases Society of America Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa).. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* , 72 7 , 1109-1116 . http://doi.org/10.1093/cid/ciab295
41) Tellier, R.., Li, Yuguo., Cowling, B.., & Tang, J.. (2019). Recognition of aerosol transmission of infectious agents: a commentary. *BMC Infectious Diseases* , 19 . http://doi.org/10.1186/s12879-019-3707-y
42) Uhlenhopp, D.., Then, E.., Sunkara, T.., & Gaduputi, V.. (2020). Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. *Clinical Journal of Gastroenterology* , 13 , 1010 - 1021 . http://doi.org/10.1007/s12328-020-01237-x
43) Umesawa, M.., & Kobashi, G.. (2017). Epidemiology of hypertensive disorders in pregnancy: prevalence, risk factors, predictors and prognosis. *Hypertension Research* , 40 , 213-220 . http://doi.org/10.1038/hr.2016.126
44) Vogt, Nicholas M.., Kerby, R.., Dill-McFarland, Kimberly A.., Harding, Sandra., Merluzzi, A.., Johnson, Sterling C.., Carlsson, C.., Asthana, S.., Zetterberg, H.., Blennow, K.., Bendlin, B.., & Rey, F.. (2017). Gut microbiome alterations in Alzheimer's disease. Scientific Reports , 7 . http://doi.org/10.1038/s41598-017-13601-y
45) Younossi, Z.., Anstee, Q.., Marietti, M.., Hardy, T.., Henry, L.., Eslam, M.., George, J.., & Bugianesi, E.. (2018). Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nature Reviews Gastroenterology & Hepatology , 15 , 11-20 . http://doi.org/10.1038/nrgastro.2017.109