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• 临床研究 •

肝衰竭患者院内感染的病原学特征 及真菌感染相关因素分析

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【摘要】 目的 探析肝衰竭患者并发院内感染的感染类型、病原菌分布情况、耐药性及真菌感染相关因素。方法 选取本院收治的168例肝衰竭并发院内感染患者为本次研究对象,同时选取80例未发生感染者为未感染组。收集患者相关临床资料,分析院内感染类型,并总结归纳肝衰竭患者并发真菌感染的相关影响因素。对疑似院内感染的肝衰竭患者,采集标本进行病原菌培养鉴定及药敏试验。结果 168例肝衰竭并发院内感染患者中,主要为腹腔感染(39.88%),其次为呼吸系统感染(30.36%)与消化系统感染(20.24%)。共检出病原菌168株,其中革兰阴性菌占比34.52%,革兰阳性菌占比20.24%,真菌占比45.24%。革兰阴性菌主要为大肠埃希菌、肺炎克雷伯菌,革兰阳性菌主要为溶血葡萄球菌、肺炎链球菌,真菌主要为白色假丝酵母菌、热带假丝酵母菌、烟曲霉。58株革兰阴性菌对庆大霉素、头孢吡辛、左氧氟沙星、环丙沙星的耐药率较高,分别为70.69%、60.34%、58.62%和55.17%,对亚胺培南、美罗培南、阿米卡星的耐药率较低,分别为3.45%、5.17%和1.72%。34株革兰阳性菌对青霉素、红霉素、左氧氟沙星、克林霉素、环丙沙星、四环素的耐药率较高,分别为100%、97.06%、70.59%、61.76%、58.82%和52.94%,未产生对万古霉素、替考拉宁的耐药株。76株真菌对氟康唑、伏立康唑、伊曲康唑的耐药率均较低,分别为19.74%、14.47%和9.21%,未产生对两性霉素B的耐药株。对比真菌感染患者与未感染患者临床资料,年龄、性别、合并高血压、合并肝性脑病差异无统计学意义($P>0.05$),合并糖尿病、侵入性操作、合并消化道出血差异有统计学意义($P<0.05$)。将上述具有统计学意义的单因素进一步进行二元 Logistic 分析发现,合并糖尿病、侵入性操作、合并消化道出血是肝衰竭患者合并真菌感染的独立危险因素($P<0.05$)。结论 肝衰竭合并院内感染患者,以腹腔感染、呼吸系统感染、消化系统感染为主。病原菌主要为白色假丝酵母菌、热带假丝酵母菌、大肠埃希菌,应根据病原学分析结果合理使用抗菌药物。合并糖尿病、侵入性操作、合并消化道出血是肝衰竭患者合并真菌感染的独立危险因素,临床上应重点关注。

【关键词】 肝衰竭;院内感染;病原学特征;真菌感染**【文献标识码】** A**【文章编号】** 1673-5234(2024)04-0482-04

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Analysis of pathogenic characteristics and fungal infection related factors of hospital acquired infections in patients with liver failure

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【Abstract】 **Objective** To explore the types of infections, distribution of pathogens, drug resistance, and factors related to fungal infections in patients with liver failure complicated by hospital acquired infections. **Methods** 168 patients with liver failure complicated by hospital acquired infections admitted to our hospital were selected as the study subjects, and 80 patients with liver failure who did not develop hospital acquired infections during the same period of treatment were selected as the uninfected group. The relevant clinical data of patients were collected, the types of hospital infections were analyzed, and the relevant influencing factors of fungal infections in patients with liver failure summarized. The specimens were collected for pathogen culture, identification and drug sensitivity testing of suspected hospital acquired liver failure patients. **Results** Among 168 patients with liver failure complicated by hospital acquired infections, the main cause was abdominal infection (39.88%), followed by respiratory system infection (30.36%) and digestive system infection (20.24%). A total of 168 strains of pathogenic bacteria were detected, of which Gram negative bacteria accounted for 34.52%, Gram positive bacteria accounted for 20.24%, and fungi accounted for 45.24%. Gram negative bacteria were mainly *Escherichia coli* and *Klebsiella pneumoniae*, Gram positive bacteria were mainly *hemolytic Staphylococcus* and *Streptococcus pneumoniae*, and fungi were mainly *Candida albicans*, *C. tropicalis*, and *Aspergillus fumigatus*. 58

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strains of Gram negative bacteria had high resistance rates to gentamicin, cefuroxime, levofloxacin, and ciprofloxacin, with resistance rates of 70.69%, 60.34%, 58.62%, and 55.17%, respectively. The resistance rates to imipenem, meropenem, and amikacin were relatively low, with resistance rates of 3.45%, 5.17%, and 1.72%, respectively. 34 Gram positive bacteria showed high resistance rates to penicillin, erythromycin, levofloxacin, clindamycin, ciprofloxacin, and tetracycline, with rates of 100%, 97.06%, 70.59%, 61.76%, 58.82%, and 52.94%, respectively. No resistant strains to vancomycin or teicoplanin were found. The resistance rates of 76 fungal strains to fluconazole, voriconazole, and itraconazole were relatively low, at 19.74%, 14.47%, and 9.21%, respectively, and no strains resistant to amphotericin B. By comparing the clinical data of patients with fungal infection and patients without fungal infection, there was no significant difference in age, sex, hypertension and hepatic encephalopathy ($P > 0.05$), but there was significant difference in diabetes, invasive procedures and gastrointestinal bleeding ($P < 0.05$). Further binary logistic analysis of the single factors with statistically significant differences in the above comparison showed that the combination of diabetes, invasive procedures, and gastrointestinal bleeding were independent risk factors for liver failure patients with fungal infection ($P < 0.05$).

Conclusion Patients with liver failure complicated by hospital acquired infections were mainly characterized by abdominal, respiratory, and digestive infections. The main pathogens were *C. albicans*, *C. tropicalis*, and *E. coli*. Antibiotics should be used reasonably based on the results of pathogen analysis. The combination of diabetes, invasive procedures, and gastrointestinal bleeding were independent risk factors for fungal infection in patients with liver failure, which should be focused on clinically.

【Key words】 liver failure; intrahospital infection; pathogenic characteristics; fungal infection

肝衰竭(Liver failure, LF)是由多种因素引发的严重肝脏损害,导致肝细胞合成、解毒、排泄等功能发生严重受损,85%以上由乙肝病毒感染引起,随着饮酒、肥胖及糖尿病的日益盛行,肝衰竭的发病率逐年上升^[1]。肝衰竭患者主要以凝血功能障碍、肝性脑病、消化道出血等各种严重并发症为主的临床症候群,患者病情凶险,病死率高达40%~90%^[2]。肝衰竭患者的肝脏各种功能严重受损,肝细胞持续损伤,出现免疫缺陷和全身性炎症导致的免疫功能障碍,导致全身炎症反应和代偿性抗炎反应,容易引发多种感染的发生^[3]。细菌或真菌感染是肝衰竭相关的最常见并发症,其中合并真菌感染的发生率约为2%~15%,呈现逐年上升的趋势^[4]。肝衰竭合并真菌感染后,对比未感染患者预后效果差,感染加剧了患者炎症的级联反应,导致多器官功能衰竭,使患者病死率进一步升高^[5]。本研究分析168例肝衰竭并发院内感染患者的临床资料,探析肝衰竭患者并发院内感染的感染类型、病原菌分布情况、耐药性及真菌感染相关因素,结果报告如下。

对象与方法

1 研究对象

选取福建省泉州市第一医院收治的168例肝衰竭并发院内感染患者为本次研究对象。男性患者118例,女性患者50例。年龄25~79(55.12±12.25)岁。其中,125例为乙型肝炎病毒感染,22例为酒精性肝病,9例为自身免疫性肝炎,6例为药物性肝炎,6例为丙型肝炎病毒感染。纳入标准:①符合中华医学会感染病学分会肝衰竭与人工肝学组制定的《肝衰竭诊疗指南(2018年版)》中关于肝衰竭相关诊断标准,被确

诊为肝衰竭^[6];②符合《医院感染诊断标准》,经腹部B超、凝血功能、肝功能及病原学检查结果,诊断为院内感染^[7];③临床资料完整。排除标准:①合并先天性或获得性免疫缺陷疾病者;②临床资料缺失;③合并恶性肿瘤或血液疾病等;④具有肝移植或骨髓抑制病史者;⑤合并精神认知功能障碍者;⑥合并艾滋病、肺结核等感染性疾病者。同时选取80例同期治疗的肝衰竭未发生院内感染患者为未感染组。

2 资料收集

通过查阅本院电子病历系统,收集患者相关临床资料,包括年龄、性别、糖尿病、高血压、有无侵入性操作(包括腹腔穿刺术、胸腔穿刺术、留置尿管、气管切开或插管等)、是否合并肝性脑病、是否合并消化道出血等。

3 病原菌鉴定及药敏试验

对疑似院内感染的肝衰竭患者,采集其血液、痰液、尿液、腹水、胸腔积液、脓液分泌物等标本置于无菌容器中,2 h内送检。将送检的标本接种于TBS肉汤中,36℃培养24~48 h,然后移种于麦凯琼脂培养基、羊血琼脂培养基上,培养24 h,挑取可疑生长菌落,获得纯培养后先经过革兰染色镜检,然后采用全自动细菌分析仪(Scan1200,美国贝克曼库尔特公司)进行病原菌种类的鉴定。采用K-B纸片扩散法进行标准化的药敏实验,药敏试验结果按照美国临床实验室标准化委员会(NCCLS)标准进行判读。

4 观察指标

①肝衰竭合并院内感染患者感染类型;②院内感染患者采集的标本中病原菌分布情况;③病原菌对临

床常见抗菌药物的耐药情况;④肝衰竭患者合并真菌感染单因素及多因素回归分析。

5 统计分析

采用 SPSS 26.0 对本次研究数据进行统计分析,计数资料采用例数、菌株和百分率(%)表示,组间对比采用 χ^2 检验,应用 Logistic 多因素回归分析影响肝衰竭患者并发真菌感染的相关因素, $P < 0.05$ 为差异有统计学意义。

结 果

1 感染类型

168 例肝衰竭并发院内感染中,67 例为腹腔感染(39.88%, 67/168),51 例为呼吸系统感染(30.36%, 51/168),34 例为消化系统感染(20.24%, 34/168),6 例为血液感染(3.57%, 6/168),5 例为泌尿系统感染(2.98%, 5/168),3 例为置管部位感染(1.79%, 3/168),2 例为口腔感染(1.19%, 2/168)。

2 病原菌分布情况

共检出病原菌 168 株,均为单一病原菌感染。革兰阴性菌共 58 株(34.52%, 58/168),包括大肠埃希菌 17 株(10.12%, 17/168),肺炎克雷伯菌 13 株(7.74%, 13/168),铜绿假单胞菌 9 株(5.36%, 9/168),产酸克雷伯菌 7 株(4.17%, 7/168),鲍曼不动杆菌 5 株(2.98%, 5/168),奇异变形杆菌 3 株(1.79%, 3/168),阴沟肠杆菌 2 株(1.19%, 2/168),粘质沙雷菌 1 株(0.60%, 1/168),褪色沙雷菌 1 株(0.60%, 1/168)。革兰阳性菌共 34 株(20.24%, 34/168),包括溶血葡萄球菌 9 株(5.36%, 9/168),肺炎链球菌 7 株(4.17%, 7/168),金黄色葡萄球菌 7 株(4.17%, 7/168),表皮葡萄球菌 5 株(2.98%, 5/168),尿肠球菌 3 株(1.79%, 3/168),粪肠球菌 2 株(1.19%, 2/168),缓症链球菌 1 株(0.60%, 1/168)。真菌共 76 株(45.24%, 76/168),包括白色假丝酵母菌 27 株(16.07%, 27/168),热带假丝酵母菌 20 株(11.90%, 20/168),烟曲霉 12 株(7.14%, 12/168),光滑假丝酵母菌 10 株(5.95%, 10/168),黄曲霉 5 株(2.98%, 5/168),克柔假丝酵母菌 2 株(1.19%, 2/168)。

3 耐药性分析

3.1 革兰阴性菌耐药性分析 对 58 株革兰阴性菌进行药敏试验,结果显示:对庆大霉素、头孢呋辛、左氧氟沙星、环丙沙星的耐药率较高,对亚胺培南、美罗培南、阿米卡星的耐药率较低。见表 1。

3.2 革兰阳性菌耐药性分析 对 34 株革兰阳性菌进行药敏试验,结果显示:对青霉素、红霉素、左氧氟沙星、克林霉素、环丙沙星、四环素的耐药率较高,未产生对万古霉素、替考拉宁的耐药株。见表 2。

表 1 革兰阴性菌耐药性分析

抗菌药物 Antibiotics	耐药菌株 Drug resistant strains	耐药率(%) Drug resistance rate
头孢呋辛	35	60.34
头孢曲松	17	29.31
头孢他啶	15	25.86
头孢吡肟	9	15.52
亚胺培南	2	3.45
美罗培南	3	5.17
环丙沙星	32	55.17
左氧氟沙星	34	58.62
阿米卡星	1	1.72
庆大霉素	41	70.69

表 2 革兰阳性菌耐药性分析

抗菌药物 Antibiotics	耐药菌株 Drug resistant strains	耐药率(%) Drug resistance rate
青霉素	34	100.00
红霉素	33	97.06
克林霉素	21	61.76
环丙沙星	20	58.82
左氧氟沙星	24	70.59
万古霉素	0	0.00
替考拉宁	0	0.00
庆大霉素	10	29.41
四环素	18	52.94
复方新诺明	15	44.12

3.3 真菌耐药性分析 对 76 株真菌进行药敏试验,结果显示,对氟康唑、伏立康唑、伊曲康唑、两性霉素 B 的耐药率分别为 19.74%(15/76)、14.97%(11/76)、9.21%(7/76)和 0。

4 肝衰竭合并真菌感染相关因素

4.1 肝衰竭合并真菌感染单因素分析 对比真菌感染患者与未感染患者临床资料,结果显示,合并糖尿病、侵入性操作、合并消化道出血对比差异具有统计学意义($P < 0.05$),年龄、性别、合并高血压、合并肝性脑病对比差异不具有统计学意义($P > 0.05$)。见表 3。

4.2 肝衰竭合并真菌感染多因素分析 以是否合并真菌感染为因变量,将上述对比差异具有统计学意义的单因素进一步进行二元 Logistic 分析,结果显示,合并糖尿病、侵入性操作、合并消化道出血是肝衰竭患者合并真菌感染的独立危险因素($P < 0.05$)。见表 4。

讨 论

肝衰竭患者免疫功能降低,容易感染多种病原体,并发院内感染已成为肝衰竭患者严重并发症之一,相关研究发现,院内感染所致肝衰竭患者死亡的风险是非感染者的 3.69 倍^[8]。通过分析肝衰竭患者并发院内感染的主要感染类型、病原菌分布特点及真菌感染的相关影响因素,有利于对患者及早确诊,可提高肝衰竭并发院内感染的防治效果,具有重要临床意义^[9]。

表3 肝衰竭合并真菌感染单因素分析
Table 3 Single factor analysis of liver failure combined with fungal infection

相关因素 Factors		真菌感染组 (n=76) Fungal infection group	未感染组 (n=80) Uninfected group	χ^2	P
年龄	<50	55	53	0.685	0.408
	≥50	21	27		
性别	男	50	59	1.173	0.279
	女	26	21		
合并糖尿病	否	53	73	11.613	0.001
	是	23	7		
合并高血压	否	50	57	0.539	0.463
	是	26	23		
侵入性操作	否	16	35	9.125	0.003
	是	60	45		
合并肝性脑病	否	56	61	0.137	0.711
	是	20	19		
合并消化道出血	否	61	79	7.289	0.007
	是	9	1		

表4 肝衰竭合并真菌感染多因素分析
Table 4 Multivariate analysis of liver failure combined with fungal infection

相关因素 Factors	β	SE	Wald χ^2 值	P	OR	OR95%CI
糖尿病	1.378	0.485	8.060	0.005	3.966	(1.532~10.264)
侵入性操作	1.003	0.384	6.822	0.009	2.726	(1.284~5.784)
消化道出血	2.489	1.104	5.088	0.024	12.053	(1.386~104.819)

本次研究中,168例肝衰竭并发院内感染患者感染类型主要为腹腔感染,其次为呼吸系统感染与消化系统感染。与许东华等^[10]研究结果相近。肝脏作为人体最大的解毒器官,尤其是肝功能分级C级的严重肝衰竭患者,存在多种器质性病变,加重肝脏免疫功能丧失,加之长期使用激素及广谱抗菌药物,机体感染风险较高^[11]。

本次研究共检出病原菌168株,主要为真菌感染,以白色假丝酵母菌、热带假丝酵母菌、烟曲霉为主。革兰阴性菌对庆大霉素、头孢吡辛、左氧氟沙星、环丙沙星的耐药率较高,对亚胺培南、美罗培南、阿米卡星的耐药率较低。革兰阳性菌对青霉素、红霉素、左氧氟沙星、克林霉素、环丙沙星、四环素的耐药率较高,未产生对万古霉素、替考拉宁的耐药株。76株真菌对氟康唑、伏立康唑、伊曲康唑的耐药率均较低,未产生对两性霉素B的耐药株。与蔡水泽等^[12]研究结果相近。氟康唑是临床上常用抗真菌药物,口服吸收良好,体内抗菌活性高于体外,但相关研究发现,氟康唑对热带假丝酵母菌、克柔假丝酵母菌的耐药率较高,临床上必须结合假丝酵母菌的鉴定结果及药敏结果来指导用药^[13]。

由于抗生素的不规范使用、反复住院及各种侵入性操作等多种原因,真菌感染在肝衰竭患者中的发病率逐年升高,因此,分析肝衰竭并发真菌感染的相关危险因素,为临床防治提供参考依据,在肝衰竭患者的诊治过程中具有重要意义。本次研究通过对比肝衰竭合并真菌感染与未感染患者的临床资料发现,年龄、性别、合并高血压、合并肝性脑病对比差异无统计学意义($P>0.05$),合并糖尿病、侵入性操作、合并消化道出血对比差异具有统计学意义($P<0.05$)。进一步分析发现,合并糖尿病、侵入性操作、合并消化道出血是肝衰竭患者合并真菌感染的独立危险因素,与马天一等^[14]研究结果相近。糖尿病患者由于血糖控制不佳,先天和获得性免疫功能受损,糖尿病患者的感染风险显著高于血糖正常患者,一项最新的研究发现,合并真菌感染的糖尿病患者病死率显著升高,长期高血糖是导致不良预后的危险因素^[15-17]。临床上针对有上述危险因素的肝衰竭患者,入院起应予以重点关注,最大限度降低感染的发生。

综上所述,肝衰竭合并院内感染患者主要为腹腔感染,病原菌以真菌为主,病原菌种类较多,临床上应根据病原学结果合理使用抗菌药物。合并糖尿病、侵入性操作、合并消化道出血是肝衰竭患者合并真菌感染的独立危险因素,具有上述症状的患者容易发生真菌感染,临床上应及时采取防治措施,降低感染率。

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