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我国贝类中人源诺如病毒检出状况的荟萃分析*

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摘要 人源诺如病毒(Human Noroviruses, HuNoVs)是引发食品安全事件的重要病原微生物。贝类为滤食性动物，是 HuNoVs 污染传播的重要媒介。本研究搜集了我国贝类污染调查的横断面研究文献，综合评价了贝类中 HuNoVs 的污染现状。通过检索中国知网、维普、万方、中国生物医学文献数据库、PubMed 和 EMbase 数据库，从所获得的 600 篇关于贝类污染 HuNoVs 相关文献中筛选纳入 37 篇。采用 Stata 14.0 软件进行荟萃分析，结果显示，我国贝类中不同基因型 HuNoVs 的混合检出率达 15% (95% CI: 11%~18%)。亚组分析显示，GⅡ基因群检出率(11%)高于GⅠ基因群(4%)；地理位置对贝类中病毒污染水平影响显著(*P*<0.01)，华南地区、华北地区、华东地区的检出率分别达到 19%、17%和 11%，而东北和西北地区则分别为 4%和 9%；此外，季节差异明显，其中，冬季的病毒检出率最高(25%)，而夏季仅为 10%，春季、秋季则分别为 16%和 12%；不同品种贝类的病毒污染同样存在差异，其中，牡蛎(Ostreidae) (16%)、贻贝(*Mytilus edulis*) (10%)和蛤(Mactridae)(9%)中病毒检出率居前三。综上所述，我国贝类中 HuNoVs 污染较为普遍，地区、季节、贝类品种等因素均对病毒污染存在显著影响。本研究结果有助于综合掌握我国贝类中食源性病毒污染现状，为精准防控食源性 HuNoVs 传播提供研判依据，促进贝类产业的高质量发展。

关键词 中国；贝类；人源诺如病毒；检出率；荟萃分析；横断面研究

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人源诺如病毒(Human Noroviruses, HuNoVs)属于杯状病毒科，是一类无包膜单股正链 RNA 病毒。根据主衣壳蛋白 VP1 的多样性，HuNoVs 被分为 10 个基因群(GⅠ-GⅩ)，其中，GⅠ、GⅡ、GⅣ、GⅧ和 GⅨ可感染人类(Chhabra *et al*, 2020)。HuNoVs 感染剂量低(十几个病毒颗粒就可造成宿主致病)、稳定性高、致病力强，是世界范围内造成人类急性肠胃炎的最常见病原，临床症状包括呕吐(87%)、腹泻(85%)和发热(56%)等，每年造成约 42 亿美元的直接医疗成本和 600 亿美元的间接成本损失(Bartsch *et al*, 2016; Lopman *et al*, 2016)。

贝类味道鲜美，具有独特的保健功能和药用价

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值，经济价值大。我国是贝类生产、加工、出口和消费大国。据《2020 年中国渔业统计年鉴》数据显示，我国贝类总产量约 1458 万 t，其中，牡蛎(Ostreidae)、贻贝(*Mytilus edulis*)和蛤蜊(Mactridae)等贝类占 70%以上(农业农村部渔业渔政管理局等，2020)。但食源性病毒污染一直是影响贝类产业健康发展的重要瓶颈问题(Yang *et al*, 2021; 白昌明等, 2021)。因贝类中检测出 HuNoVs 而导致产品被召回的事件时有发生，造成了严重的经济损失。贝类属于滤食性动物，通过生物积累过程将养殖水体中的病原微生物吸附至体内(宿志伟等, 2016)。此外，HuNoVs 富集于贝类体内后很难通过常规净化手段去除(Battistini *et al*, 2021; Rupnik *et al*, 2021)。因此，食用生的或未经过适当煮熟的受污染贝类易导致急性肠胃炎暴发。

我国近年来对贝类中 HuNoVs 污染的重视程度不断提高，多个省份均陆续开展了相关风险监测，但上述研究多集中在某一区域、部分季节、部分品种，研究结果分散，不利于全面掌握我国贝类 HuNoVs 污染现状。荟萃分析是将多个目的相同的研究结果进行合并分析的统计学方法。因此，本研究搜集有关中国贝类污染调查的横断面研究，用荟萃分析系统归纳我国近年来贝类中检出 HuNoVs 的现状，针对贝类采样的地区、季节以及种类等差异进行系统分析。本研究结果有助于在大空间范围、大时间跨度的视角下了解我国贝类中 HuNoVs 污染风险现状，从而为我国经济贝类中食源性病毒的精准防控提供数据支撑。

1　资料与方法

1.1　纳入与排除标准

1.1.1　研究类型　　横断面研究。

1.1.2　研究对象　　中国地区受 HuNoVs 污染的贝类。

1.1.3　效应量(effect size)　　检出率。

1.1.4　排除标准　　重复发表的文献；研究设计不符合纳入标准；数据不全且无法获得；被多篇文章重复发表的同一批数据等。

1.2　文献检索策略

计算机检索中国知网、维普、万方、中国生物医学文献数据库、PubMed、Web of Science、Embase 和 Cochrane Library 数据库，搜集关于我国贝类中 HuNoVs 污染情况的横断面研究，检索时限均为建库至 2021 年 12 月 31 日。检索采取主题词和自由词相结合的方式，检索策略根据不同数据库进行调整。中文检索词包括诺如病毒、诺瓦克病毒、海产品、贝类、双壳贝类、牡蛎、生蚝、贻贝、青口(*Perna viridis*)、蛤、扇贝和蚶。英文检索词包括 norovirus、norwalk virus、seafood、shellfish、bivalves、oyster、mussel、cockle、scallop、clam 和 China。以 PubMed 为例，具体检索策略见图 1，文献筛选流程及结果见图 2。

#1	norovirus [Mesh]
#2	norwalkvirus
#3	#1 OR #2
#4	seafood [Mesh]
#5	shellfishOR bivalves OR oyster OR mussel OR cockle OR scallop OR clam
#6	#4 OR #5
#7	China
#8	#3 AND #6 AND #7

图 1　PubMed 检索策略

Fig.1　Retrieval strategy in PubMed

1.3　资料提取

对拟纳入的文献进行详细阅读，资料提取内容主要包括：①纳入研究的基本信息，包括文献题目、第一作者、发表时间等；②研究对象的基本特征，包括各文献的研究省份、贝类种类、调查样本数、检测方法、HuNoVs 基因群、季度分布等关键信息。

1.4　统计分析

采用 Stata 14.0 软件进行荟萃分析。采用 Q 检验(P 值)和 I^2 分析研究的异质性，若 $P>0.10$ 且 $I^2\leqslant 50\%$，则采用固定效应模型；若 $P<0.10$ 且 $I^2>50\%$，则采用随机效应模型。效应量为 HuNoVs 的检出率，并提供其 95%置信区间(confidence interval, CI)。按照 HuNoVs 基因群、地区分布、季节分布和贝类种类进行亚组分析。最后，采用 Begg's 检验对文献发表偏倚进行评估。

2　结果

2.1　纳入文献基本情况

本次分析纳入的 37 篇文献中，均为横断面研究。单项研究中最大的样本数量为 2955 份，最小为 52 份。表 1 记录了各个地区纳入的文献数量，表 2 总结了纳入文献的具体信息。

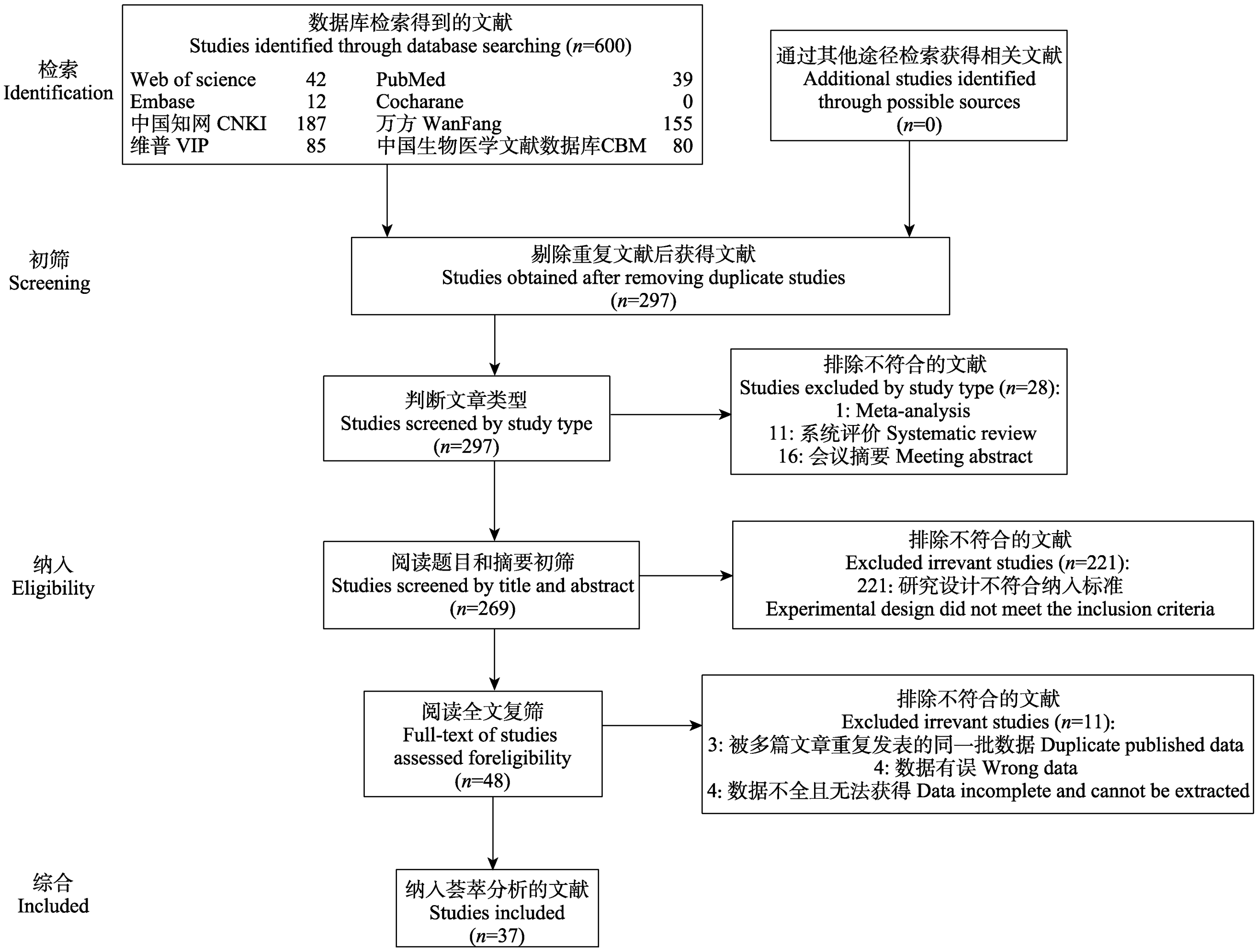

图 2　文献筛选流程

Fig.2　Flow chart of the search strategy and selection of studies

2.2　荟萃分析结果

共纳入 37 篇文献，总样本量 17 162 份，HuNoVs 污染的贝类有 1 970 份。基于随机效应进行荟萃分析，得出 37 个研究汇总的效应量 0.15，95%置信区间为 0.11~0.18，异质性检验 $P<0.01$，$I^2=97.22\%$，具有统计学意义。具体情况见以下森林图(图 3)。

2.3　亚组分析结果

以基因群、地区、季度和贝类种类作为分组因素进行亚组分析，结果如表 3 所示，各个亚组内和亚组间的检出率差异均有统计学意义($P<0.01$)，但同时各亚组均存在较高的异质性($I^2>50\%$)，故均采用随机效应模型合并效应量。在贝类中，单一 GⅠ基因群污染、单一 GⅡ基因群污染以及 GⅠ和 GⅡ基因群混合污染的检出率分别为 3%、10%和 1%；不同地区的病毒污染水平差异显著，其中，华南地区(广东省、广西壮族自治区、海南省)检出率高达 19%，华北(北京市、河北省)和华东地区(福建省、江苏省、山东省、上海市、浙江省)的检出率次之，分别为 17%和 11%，西北(甘肃省)和东北(辽宁省)地区的检出率最低，分别为 9%和 4%；病毒污染水平有明显的季节性差异，春季、夏季、秋季和冬季的检出率分别是 16%、10%、12%和 25%；不同贝类种类的病毒污染水平存在明显差异，牡蛎、贻贝和蛤的检出率相对较高，分别是 16%、10%和 9%，而蚶和蛏的检出率均为 5%，扇贝的检出率仅为 4%。

3　讨论

HuNoVs 是引发全球食品安全事件的重要病原，其中，受污染的贝类是其重要媒介之一。我国作为贝类生产消费大国，有必要定期对贝类进行病毒监测，了解中国不同地区、不同季节、不同贝类的 HuNoVs 污染差异。本研究严格按照文献的纳入和排除标准进行文献的筛选，纳入文献的研究样本达 17 162 份，

涉及多个省份和地区，相对于单个的横断面调查，更具有代表性。国家标准 GB 4789.42-2016 规定了食品中 HuNoVs 的检测方法是实时荧光定量 PCR (Real-time quantitative PCR，RT-qPCR)。在 37 项纳入研究中，大部分研究(32 项)采用了 RT-qPCR 方法对贝类中 HuNoVs 进行定量检测。另外，有 5 项研究仅通过逆转录(巢式)PCR 法结合凝胶电泳的方法判断贝类的核酸样本是否扩增出目的条带或测序分型，也被纳入了本次荟萃分析。

经荟萃分析发现，我国贝类中食源性 HuNoVs 的检出率达 15%。接着，从贝类采样的地区、季节以及种类等分别进行亚组分析。需要说明的是，部分研究由于没有区分具体的 HuNoVs 基因群、采样地区不局限于中国地理大区、季节数据无法提取等，未纳入相应的亚组。HuNoVs 具有多样性，亚组分析结果显示，单一 GⅠ或 GⅡ基因群的检出率分别为 3%和 10%，GⅠ和 GⅡ基因群的混合检出率为 1%。就优势基因群而言，贝类与水环境和临床监测的结果一致。关于全球范围内水源中的 HuNoVs 污染的荟萃分析结果显示，GⅠ基因群、GⅡ基因群及 GⅠ和 GⅡ基因群混合污染的检出率分别为 16%、20.6%和 12.8% (Ekundayo *et al*, 2021)。此外，有研究评估了发展中国家急性胃肠炎的患病率，显示 HuNoVs 的总患病率为 17%，其中，GⅡ基因群的患病率(15%)高于 GⅠ基因群(1%)(Nguyen *et al*, 2017)。综合以上分析，HuNoVs 在人群、环境和食品中很可能存在循环传播路径。

表 2 详细记录了各项研究中贝类样本的来源，其中有 35 项研究集中在某一省份，有 2 项研究多于一个省份(Tao *et al*, 2018; Ma *et al*, 2013)。将各项研究的样本来源按我国的地理大区进行归纳，显示主要集中在华南和华东地区(表 1)。本研究结果显示，不同地区贝类中 HuNoVs 的污染水平存在差异。具体来说，华南(广东省、广西壮族自治区、海南省)和华北地区，(北京市、河北省)的检出率分别为 19%和 17%；华东(福建省、江苏省、山东省、上海市、浙江省)、西北(甘肃省)和东北(辽宁省)地区的检出率较低，分别为 11%、9%和 4%。可能的原因如下：华南(10 项)、华北(9 项)和华东(18 项)地区对贝类进行了更多的 HuNoVs 检测，因此，报告的检出率更高。而东北和西北地区仅各有 2 项研究，因此，监测的贝类样本数量有限。虽然贝类主要养殖于沿海地区，但其销售范围遍布全国各地。这一现象说明目前关于我国非沿海地区的市售贝类中病毒监测的数据较少，容易使消费者低估或忽视当地贝类中病毒污染的食用风险。实际上，贝类的生产条件在不同地区之间可能存在很大差异，农业投入和技术、HuNoVs 的流行病学特点、养殖用水质量、运输渠道及加工方式等情况均可能会影响贝类中病毒污染的发生和水平。

表 1 我国不同地区纳入的文献数量

Tab.1 The number of included articles in different regions of China

地区名称 Geograhical names	纳入文献数量 Number of included articles
北京市 Beijing	7
广东省 Guangdong Province	5
浙江省 Zhejiang Province	5
江苏省 Jiangsu Province	4
山东省 Shandong Province	4
福建省 Fujian Province	3
甘肃省 Gansu Province	2
广西壮族自治区 Guangxi Zhuang Autonomous Region	2
河北省 Hebei Province	2
辽宁省 Liaoning Province	2
上海市 Shanghai	2
河南省 Henan Province	1

不同季节的贝类的 HuNoVs 污染水平存在较大差异。冬季(25%)和春季(16%)的检出率高于夏季(10%)和秋季(12%)。水温低于 5 ℃和较大的污水排放量已被证实是贝类 HuNoVs 污染的主要风险因素(Campos *et al*, 2017)。冬季缺乏紫外线、环境温度低，给 HuNoVs 的存活提供了良好的条件。同时，该季节是贝类的收获季节，消费量激增。在广东省进行的一项研究探讨了季节对 HuNoVs 检出率的影响。冬季和春季期间在养殖水体(20.0%)、牡蛎(50.0%)和肠胃炎病例(20.7%)中检测到更多 HuNoVs，而夏季和秋季的检出率分别为 6.2%、10.9%和 17.6% (王安娜等, 2016)。另外，系统发育分析显示出相同基因型 HuNoVs 在养殖水体、海产品和人群之间的循环，证实了水源、食品和人群之间存在密切的相关性(王安娜等, 2016)。我国 HuNoVs 感染导致的疫情暴发具有明显的季节性，多以春季和秋冬季为高发。大多数疫情发生在较冷的季节。2013—2014 年广西壮族自治区暴发疫情主要集中在 3 月、10 月和 11 月(王晶等, 2016)，广东省则主要发生在冬季和春季(杨芬等, 2017)；2016 年北京市疫情集中在春季和冬季(蔡伟等, 2018)；2015—2016 年河北省疫情主要发生在 4—6 月和 12 月(刘莹莹等, 2017)；2018—2019 年福建省漳州市暴发疫情的季节高峰主要在 2—3 月和 9—12 月(郭丽清等, 2020)。位于中国西南部的青藏高原 HuNoVs 感染率非常低

表 2　贝类中人源诺如病毒检出率的荟萃分析中纳入研究的详细信息

Tab.2　Detailed information of the studies included in meta-analysis of the human noroviruses detected in shellfish

纳入研究 Included studies	采样地区 Sampling area	样品总数 Sample size	检出总数 Total number of contaminated samples	G Ⅰ^a	G Ⅱ^b	G Ⅰ&G Ⅱ^c	检测方法 Detection method
杨家乐等(2022)	广东(广州) Guangdong (Guangzhou)	110	58	/	58	/	实时荧光定量 PCR (RT-qPCR)，逆转录巢式 PCR (reverse transcription-nested PCR, RT-nPCR)
吴立梦等(2021)	上海 Shanghai	580	52	13	34	5	RT-qPCR, RT-nPCR
贾添慧等(2021)	上海 Shanghai	633	140	79	60	1	RT-nPCR
王永全等(2021)	北京 Beijing	72	25	3	20	2	RT-qPCR, RT-nPCR
朱晓露等(2021)	江苏(连云港) Jiangsu (Lianyungang)	180	48	9	32	7	RT-qPCR
刘雪杰等(2021)	福建 Fujian	211	64	13	29	22	RT-qPCR
Zhang 等(2021a)	山东(乳山) Shandong (Rushan)	356	60	26	19	15	RT-qPCR, RT-nPCR
时沙沙等(2020)	浙江(舟山) Zhejiang (Zhoushan)	670	66	37	29	0	RT-nPCR
严寒秋等(2020)	北京 Beijing	72	20	16	2	2	RT-nPCR
刘永华等(2020)	辽宁(盘锦) Liaoning (Panjin)	1465	53	/	/	/	RT-nPCR
张乐(2020)	广东(广州) Guangdong (Guangzhou)	52	19	/	19	/	RT-qPCR
刘志婷等(2019)	广东(广州、湛江等) Guangdong (Guangzhou, Zhanjiang, *et al.*)	1298	217	28	116	73	RT-qPCR
刘雪杰等(2019)	福建(福州、厦门) Fujian (Fuzhou, Xiamen)	240	26	/	/	/	RT-qPCR
白雪等(2018)	河北(石家庄、秦皇岛等) Hebei (Shijiazhuang, Qinhuangdao, *et al.*)	691	42	16	22	4	RT-qPCR
严寒秋等(2018)	北京 Beijing	56	21	0	20	1	RT-qPCR, RT-nPCR
李羽翡等(2018)	甘肃(兰州) Gansu (Lanzhou)	55	5	0	5	0	RT-qPCR
寇晓霞等(2018)	广东(广州、珠海等) Guangdong (Guangzhou, Zhuhai, *et al.*)	290	50	18	32	0	RT-qPCR
王虹玲等(2018)	浙江(舟山) Zhejiang (Zhoushan)	468	19	0	19	0	RT-qPCR
Tan 等(2018)	广西 Guangxi	463	96	2	94	0	RT-qPCR
Tao 等(2018)	北京、山东 Beijing, Shandong	652	135	29	85	21	RT-qPCR
王佳慧等(2017)	北京 Beijing	293	27	10	17	0	RT-qPCR

续表

纳入研究 Included studies	采样地区 Sampling area	样品总数 Sample size	检出总数 Total number of contaminated samples	GⅠ^{a}	GⅡ^{b}	GⅠ&GⅡ^{c}	检测方法 Detection method
倪云龙等(2017)	江苏(无锡、江阴等) Jiangsu (Wuxi, Jiangyin, *et al.*)	657	100	12	55	33	RT-qPCR
李平等(2017)	海南(海口) Hainan (Haikou)	220	6	0	2	4	RT-qPCR
江涛等(2017)	北京 Beijing	356	57	12	39	6	RT-qPCR
骆海朋等(2017)	北京 Beijing	478	40	4	36	0	RT-qPCR
吕素玲等(2017)	广西(北海) Guangxi (Beihai)	480	53	0	53	0	RT-qPCR
闫鑫等(2017)	河北(秦皇岛) Hebei (Qinhuangdao)	60	11	1	10	0	RT-qPCR
白颉等(2016)	浙江(宁波、温州等) Zhejiang (Ningbo, Wenzhou, *et al.*)	2 955	63	0	63	0	RT-qPCR
王安娜等(2016)	广东(珠海) Guangdong (Zhuhai)	331	108	50	6	52	RT-qPCR, RT-nPCR
柯明月等(2015)	福建(厦门) Fujian (Xiamen)	198	45	12	19	14	RT-qPCR
高见等(2013)	浙江(杭州、台州等) Zhejiang (Hangzhou, Taizhou, *et al.*)	116	9	0	9	0	RT-qPCR
徐奋奋等(2013)	浙江(宁波) Zhejiang (Ningbo)	124	11	0	11	0	RT-qPCR
梁辉等(2013)	广东(广州、湛江等) Guangdong (Guangzhou, Zhanjiang, *et al.*)	275	41	11	17	13	RT-qPCR
Ma 等(2013)	辽宁、甘肃、山东、江苏 Liaoning, Gansu, Shandong, Jiangsu	840	112	/	112	/	RT-qPCR, 逆转录PCR (reverse transcription-PCR, RT-PCR)
柯丹枫等(2012)	广东(湛江、茂名等) Guangdong (Zhanjiang, Maoming, *et al.*)	390	39	11	26	2	RT-qPCR
李海波等(2011)	江苏(南通) Jiangsu (Nantong)	129	2	/	/	/	RT-qPCR
李振(2007)	山东(青岛) Shandong (Qingdao)	646	30	/	/	/	RT-PCR

注：a：仅检出GⅠ；b：仅检出GⅡ；c：同时检出GⅠ和GⅡ；/：未报道。

Note: a: Only GⅠ was detected; b: Only GⅡ was detected; c: Both GⅠ and GⅡ were detected; /: No relevant data.

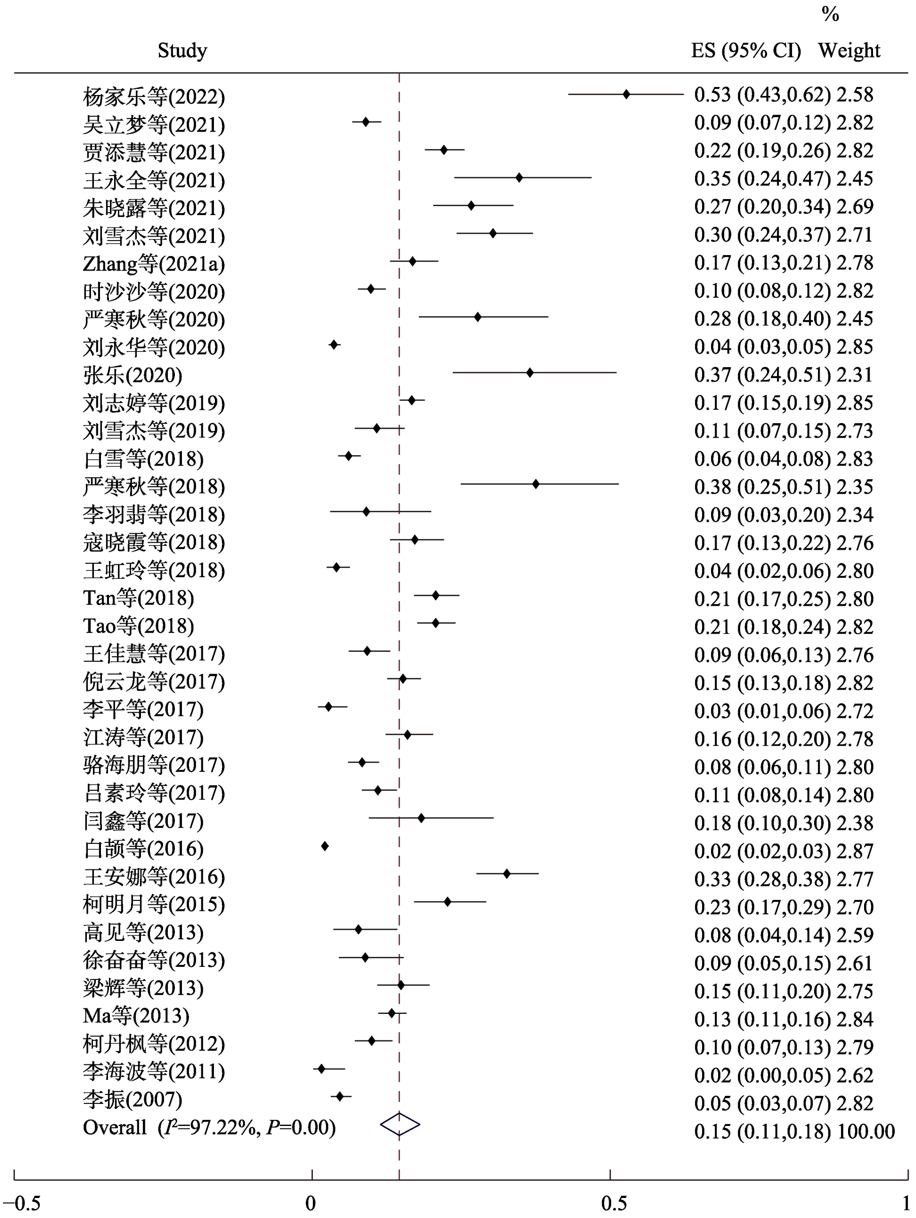

图 3　贝类中人源诺如病毒检出率的荟萃分析的森林图

Fig.3　Forest map of the meta-analysis of human noroviruses detected in shellfish

(余建兴等, 2015)，可能与该地区不常食用贝类的饮食习惯有一定联系。

我国不同贝类中 HuNoVs 污染水平存在差异。在所有的贝类中，牡蛎是被研究最多的品种，同时也是 HuNoVs 检出率最高的(16%)。究其原因，牡蛎产量高，是占目前生食比例较大的品种，并且近年来有逐渐增多的趋势。另外，牡蛎的养殖场所位于浅海湾，容易受生活污水的污染。此外，牡蛎的不同组织中均含有 HuNoVs 的受体(类组织血型抗原)(Tian *et al*, 2008)和病毒吸附介质(热休克蛋白 70)(Zhang *et al*, 2021b)，可特异性结合 HuNoVs (Wang *et al*, 2008a; Wang *et al*, 2008b)，导致牡蛎污染病毒含量可达到周围养殖水体的几十倍到上千倍(Yang *et al*, 2021)。因此，食用加工不当的牡蛎可能更容易引发食品安全事件。2014 年上海美食节引发了一起食品安全事件，83%的病例与牡蛎消费有关，其中 GⅡ.4 Sydney_2012、GⅡ.13、GⅠ.2、GⅠ.5 为主要基因型(Wang *et al*, 2015)。牡蛎养殖区人群长期生活在高风险环境中，且伴有高危饮食习惯，HuNoVs GⅡ.17 血清抗体总阳性率高达 88.2% (172/195)(覃霖, 2017)。

由于单个率荟萃分析的特点，本研究所纳入研究存在较高的异质性($I^2 > 50\%$)；纳入研究均为横断面研究，受纳入研究的研究设计所限，如样本数量、贝类前处理方法和检测方法存在差异，多种偏倚无法避

表3 贝类中人源诺如病毒检出率的亚组荟萃分析结果汇总

Tab.3 Summary of subgroup meta-analysis of human noroviruss detected in shellfish

亚组分析 Subgroup	文献数量 Number of studies	样本总数 Number of samples	检出率 Prevalence (95%CI)	异质性检验 Heterogeneity test		效应模型 Effect model	亚组间比较(*P* 值) Differences between subgroups (*P*-value)	发表偏倚 Publication bias
				I^2(%)	*P*-value			Begg's 检验 Begg's test
基因群 Genogroup							<0.01	
G Ⅰ[a]	30	13 680	0.03 (0.01~0.04)	95.63	<0.01	随机 Random		0.35
G Ⅱ[b]	33	14 682	0.10 (0.08~0.13)	95.41	<0.01	随机 Random		0.05
G Ⅰ &G Ⅱ[c]	30	13 680	0.01 (0.01~0.03)	95.10	<0.01	随机 Random		0.04
地区 Area							<0.01	
东北 Northeast China	1	1 465	0.04 (0.03~0.05)	0	<0.01	–		–
华北 North China	8	2 078	0.17 (0.11~0.25)	92.96	<0.01	随机 Random		0.05
华东 East China	15	8 163	0.11 (0.07~0.17)	97.65	<0.01	随机 Random		0.62
华南 South China	10	3 909	0.19 (0.13~0.26)	95.78	<0.01	随机 Random		0.60
西北 Northwest China	1	55	0.09 (0.03~0.20)	0	<0.01	–		–
季节 Season							<0.01	
春 Spring	22	2 478	0.16 (0.12~0.20)	84.97	<0.01	随机 Random		0.41
夏 Summer	24	3 999	0.10 (0.07~0.13)	86.90	<0.01	随机 Random		0.65
秋 Fall	25	2 848	0.12 (0.08~0.17)	90.76	<0.01	随机 Random		0.04
冬 Winter	22	1 949	0.25 (0.18~0.33)	92.74	<0.01	随机 Random		0.20
种类 Species							<0.01	
牡蛎 Oyster	32	8 799	0.16 (0.13~0.20)	93.90	<0.01	随机 Random		0.41
贻贝 Mussel	14	2 589	0.10 (0.06~0.15)	91.33	<0.01	随机 Random		0.10
扇贝 Scallop	10	1 079	0.04 (0.01~0.09)	88.78	<0.01	随机 Random		0.24
蛤 Cockle	11	2 169	0.09 (0.03~0.18)	96.52	<0.01	随机 Random		0.44
蚶 Blood clam	12	1 478	0.05 (0.02~0.08)	70.69	<0.01	随机 Random		0.38
蛏 Razor clam	8	861	0.05 (0.00~0.14)	91.67	<0.01	随机 Random		0.71
其他 [d]Other	4	187	0.01 (0.00~0.17)	85.14	<0.01	随机 Random		0.73

注：a：仅检出 G Ⅰ；b：仅检出 G Ⅱ；c：同时检出 G Ⅰ 和 G Ⅱ；d：包含螺、江珧和龟足；–：不涉及。

Note: a: Only G Ⅰ was detected; b: Only G Ⅱ was detected; c: Both G Ⅰ and G Ⅱ were detected; d: Including snail, pen shell, and Japanese goose barnacle; –: Not involved.

免。此外，大多数纳入研究没有报告定量限的信息，这使得不同实验室数据的比较变得困难。

食源性病毒污染已成为影响我国贝类产业健康发展的重要因素之一。目前，基于污水和贝类的净化处理工艺仅对大多数细菌污染物有效，而对病毒的净化效率较低，因此，与病毒相关的胃肠炎和肝炎暴发持续存在(Marsh *et al*, 2018)。考虑到贝类消费的健康益处、全球人口增加以及粮食需求增加，保障贝类产品安全至关重要。“从海洋到餐桌”、“从码头到菜品”，受食源性病毒污染贝类的危害性需得到更广泛的认识。

本研究是首次对我国贝类 HuNoVs 污染水平的系统性回顾。研究表明，可以通过监测贝类的 HuNoVs 污染情况来揭示当地流行病学的可行性和重要性。未来，需要完善“人–环–食”链条中食源性病毒污染监测网络，建立精准的防控技术体系，从而保障我国贝类产业良性发展以及消费者健康。

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Detection of Human Noroviruses in Shellfish in China: A Meta-Analysis

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Abstract Human norovirus (HuNoV) is a non-enveloped, single-stranded, positive-stranded RNA virus belonging to the family Caliciviridae. HuNoVs are important pathogenic microorganisms responsible for causing food safety incidents. Numerous species of shellfish are characterized by their abundant nutritional value, excellent healthcare function, and a high economic value. As a filter-feeding animal, shellfish filter the seawater at a rate of 4–20 L per hour and ingest microalgae to meet their physiological needs. Additionally, shellfish are able to continuously accumulate viruses from seawater into their bodies, resulting in a concentration ten or even thousand times higher in their tissues than in the environment. In recent years, more attention has been paid to HuNoV contamination in shellfish in China, and related monitoring studies have been conducted in different areas. However, most of these studies focused on a certain region in a certain period of time, and some species, which are not conducive to a comprehensive understanding of the overall prevalence of HuNoVs in shellfish in China. Meta-analysis refers to the methods which focus on contrasting and combining results from different studies for identifying patterns among the study results or other interesting relationships that may come to light in the context of multiple studies. This study aimed to collect cross-sectional data on the studies conducted on shellfish contamination in China. The search terms used were Norwalk virus, norovirus, shellfish, bivalves, oysters, mussels, clams, cockles, and scallops in all the databases (CNKI, VIP, CBM, WanFang Data, PubMed, Web of Science, Embase, and Cochrane Library). A total of 600 studies on HuNoV

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contamination of shellfish were initially included in the data. First, 303 duplicate studies were removed, leaving 297 studies remaining. One meta-analysis, 11 reviews, and 16 meeting abstracts were excluded from the first analysis. In the second analysis, abstracts of the remaining 269 studies were read by two independent reviewers, further excluding 221 studies in which experimental designs did not meet the inclusion criteria. After carefully reading the full text of the 48 studies, 11 of them were excluded. Ultimately, 37 studies were included in the final analysis. The total sample size in these 37 studies was 17 162 among which the maximum number of samples in a single study was 2 955, and the minimum was 52, and the total number of HuNoV-contaminated samples was 1 970. The meta-analysis was conducted using Stata 14.0, and the effect size was defined as the prevalence of HuNoVs (percentage). Moreover, the heterogeneity of the studies was examined using Q test (P-value) and I^2. The pooled prevalence of HuNoVs in shellfish was found to be 15% with an I^2 value of 97.22%, which indicated a strong heterogeneity among the 37 studies. We then grouped them based on genogroups, area, season, and species using a random effect model. As a result, GⅠ and GⅡ were found as the two most prevalent genogroups. As revealed by the results, the prevalence of contamination of GⅠ alone, contamination of GⅡ alone, and the combined contamination of GⅠ and GⅡ was found to be 3%, 10%, and 1%, respectively; both Beijing and Guangdong contributed the most with seven studies, followed by Zhejiang with five studies. In addition, there were four studies conducted each in Jiangsu and Shandong, and Fujian contributed with three studies. Two studies were conducted in Gansu, Guangxi, Hebei, Liaoning, and Shanghai. Only one study has been conducted in Hainan. The geographical location exhibited a significant impact on the prevalence of HuNoVs ($P<0.01$), and its prevalence in South China (Guangdong, Guangxi, Hainan), North China (Beijing, Hebei), and East China (Fujian, Jiangsu, Shandong, Shanghai, and Zhejiang) reached 19%, 17%, and 11%, respectively, while those in Northeast China (Liaoning) and Northwest China (Gansu), which were not coastal areas, were 4% and 9%, respectively. HuNoVs contamination in shellfish was found to be significantly correlated with the season. At low temperatures, the virus is more persistent, and shellfish metabolism may be inhibited. Our results showed that the prevalence of HuNoVs was the highest in winter (25%), only 10% in summer, and 16% and 12% in spring and autumn, respectively. HuNoVs may contaminate a wide variety of species during the pre-harvest or post-harvest stages. Oysters, clams, and mussels have been recognized as the most common seafood on the table and therefore these are the most investigated. The results of this meta-analysis revealed that the prevalence of HuNoVs in oysters, mussels, and clams was 16%, 10%, and 9%, respectively. The possible reasons why oysters showed the highest prevalence among all shellfish are as follows. One, the oyster farming area is located in shallow bays, which are easily contaminated by domestic sewage. Second, different oyster tissues contain HuNoV receptors (human histo-blood group antigens (HBGAs)-like carbohydrates) and protein-ligands (oyster heat shock protein 70), which can specifically bind to HuNoVs. In summary, HuNoV contamination in shellfish is common in China, and the region, season, and species exhibit significant effects on the prevalence of HuNoVs. The results of this study are beneficial for gaining insights into the HuNoV contamination in shellfish, demonstrating the importance of continuous HuNoV monitoring. Future studies should establish some effective control measures to ensure the sound growth of the shellfish industry in China.

Key words　China; Shellfish; Human noroviruses; Prevalence; Meta-analysis; Cross-sectional studies