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A review of diarrhoea aetiology in Papua New Guinea, 1995-2012

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SUMMARY

The large contribution of diarrhoea to morbidity and mortality rates in Papua New Guinea (PNG) warrants a significant response to diagnosing aetiology, determining appropriate management and reducing risk factors that facilitate transmission of enteric pathogens. We conducted a review of literature to assess the extent of research published on the aetiology of diarrhoea in PNG between 1995 and 2012. Of 54 peer-reviewed articles that were selected for review, 25 pertained to aetiology. While the majority of articles described typhoid fever and non-typhoid salmonellosis, shigellosis, rotavirus, pigbel and cholera were also represented in the literature reviewed.

Introduction

Diarrhoea remains an important cause of morbidity and mortality in Papua New Guinea (PNG). National health statistics (2007-2008) continue to report diarrhoea as a leading reason for outpatient attendance (4.4%) and admission (5.1%) at health facilities throughout the country (1). Diarrhoea is also a leading cause of mortality (5.8%) in PNG (1), particularly in children less than five years of age (2,3). One study conducted at Port Moresby General Hospital (PMGH) reported a case fatality rate (CFR) of 3.9% among children admitted with severe diarrhoea (4). At Goroka Provincial Hospital, diarrhoea was reported as the cause of death in 9.3% of paediatric deaths between 1998 and 2000 (5). The large contribution of diarrhoea to morbidity and mortality rates in the country warrants a significant response in diagnosing the causes (aetiology), determining appropriate management including antimicrobial susceptibility patterns of aetiological agents (where such treatment is appropriate) and reducing risk factors that facilitate transmission of enteric pathogens.

Information on the aetiology of diarrhoea, antimicrobial susceptibility patterns and risk factors is not only beneficial for individual patient management but also critical for public health strategies aimed at reducing morbidity and mortality caused by diarrhoea at a population level. Thus the purpose of this review is to assess the extent of research published on diarrhoea aetiology in PNG since the last special issue on enteric infections was published in March 1995 by this Journal, to summarize this published evidence and to highlight gaps in order to guide future research.

Methods

We conducted a review of literature on diarrhoea aetiology in PNG published between 1995 and 2012. Literature had to be peer-reviewed and in English to be included. In March 2013, we conducted searches in PubMed using the following medical subject heading (MeSH) terms: 'diarrh* AND Papua New Guinea', 'enteri* AND Papua New Guinea', 'gastr* AND Papua New Guinea', 'typhoid AND Papua New Guinea', 'salmonella AND Papua New Guinea', 'shigell* AND Papua New Guinea', 'choler* AND Papua New Guinea', 'cryptosporidium AND Papua New Guinea', 'escherichia coli AND Papua New Guinea' and 'parasit* AND diarrh* AND Papua New Guinea'.

The titles and abstracts of all hits generated through the searches were reviewed and

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articles not relevant to diarrhoea aetiology in PNG were omitted to assemble a preliminary list of literature. The preliminary articles were then reviewed in full and a final list of literature pertaining to diarrhoea aetiology in PNG was assembled for analysis.

Results

The searches conducted in PubMed generated a total of 142 hits. After an initial screen of titles and/or abstracts and removal of non-relevant articles, the preliminary list consisted of 89 articles. Following a full review of articles in the preliminary list and removal of duplicates, 54 articles were selected as relevant to the scope of this review. Table 1 presents a summary of the hits generated for the different MeSH searches.

Articles selected for review were categorized into groups according to their

TABLE 1

RESULTS OF MESH SEARCHES CONDUCTED TO FACILITATE THE REVIEW OF DIARRHOEA AETIOLOGY IN PAPUA NEW GUINEA

MeSH search term	Number of hits	Number of articles selected as relevant for preliminary list	Number of articles selected after full review
diarrh* AND Papua New Guinea	39	26	24
enteri* AND Papua New Guinea	38	13	12
gastr* AND Papua New Guinea	7	5	4
typhoid AND Papua New Guinea	19	14	14
salmonella AND Papua New Guinea	12	10	9
shigell* AND Papua New Guinea	4	4	4
choler* AND Papua New Guinea	4	3	3
cryptosporidium AND Papua New Guinea	3	2	2
escherichia coli AND Papua New Guinea	11	9	6
parasit* AND diarrh* AND Papua New Guinea	5	3	3
Total	142	89	81
		Number of duplicates omitted	24
		Number of articles not able to be retrieved	3
		Total number of articles for analysis	54

MeSH = medical subject heading

primary focus, aims and objectives. A total of 25 articles were directly relevant to aetiological agents that caused diarrhoea among other symptoms. Figure 1 presents the categorization of selected articles.

Overview of published research on diarrhoea aetiology in Papua New Guinea

The focus of published research on aetiology in PNG over the last 18 years may not necessarily reflect the actual burden of diarrhoea caused by particular aetiological agents. The primary reason is that diarrhoea research in PNG has been somewhat haphazard over the last couple of decades. The published literature can be summarized into two categories: those pertaining to typhoid and its causative agent *Salmonella enterica* serovar Typhi [10/25] and those describing other aetiologies [13/25]. The primary health concern associated with typhoid fever is febrile illness; however, we felt that it was important to include research on typhoid in this review as it can cause diarrhoea and its transmission and persistence within the community is similar to that of other enteric pathogens.

Of the remaining two articles, one study was conducted in the highlands of PNG and had the primary aim of determining the burden caused by viral, bacterial and parasitic agents in children with diarrhoea (6). Another, also conducted in the highlands, investigated the aetiology of child mortality, which included diarrhoea (5). The study by Howard et al. (6) actually commenced more than 25 years ago. However, it was published within the time frame of this review and provides the most comprehensive information on diarrhoea aetiology to date. This highlights the limited research conducted on diarrhoeal aetiology despite the significant contribution of diarrhoeal diseases to national morbidity and mortality rates.

Studies describing various other aetiologies include research on *Shigella* spp. [2/13] (7,8), rotavirus [1/13] (9) and, most recently, *Vibrio cholerae* [2/13] (10,11). Research on intestinal helminths [2/13] (12,13) and spirochaetes [1/13] (14) was also represented although these two agents may not always cause diarrhoea. One study investigated to what extent pigbel (enteritis necroticans) was still a concern in the highlands of PNG (15). Finally, the importance of diarrhoea associated with other infections, notably measles [1/13] (16) and HIV [3/13] (17-19), was also reported in the published literature.

Typhoid fever and non-typhoid salmonellosis

In 1995, Passey et al. reported on the emerging problem of typhoid fever in the highlands of PNG (20,21). The findings of their 12-month prospective study showed an annual case rate of 1208 per 100,000 population (20). The culture positivity rate they reported was lower at 817 per 100,000 population but there was no doubt at the

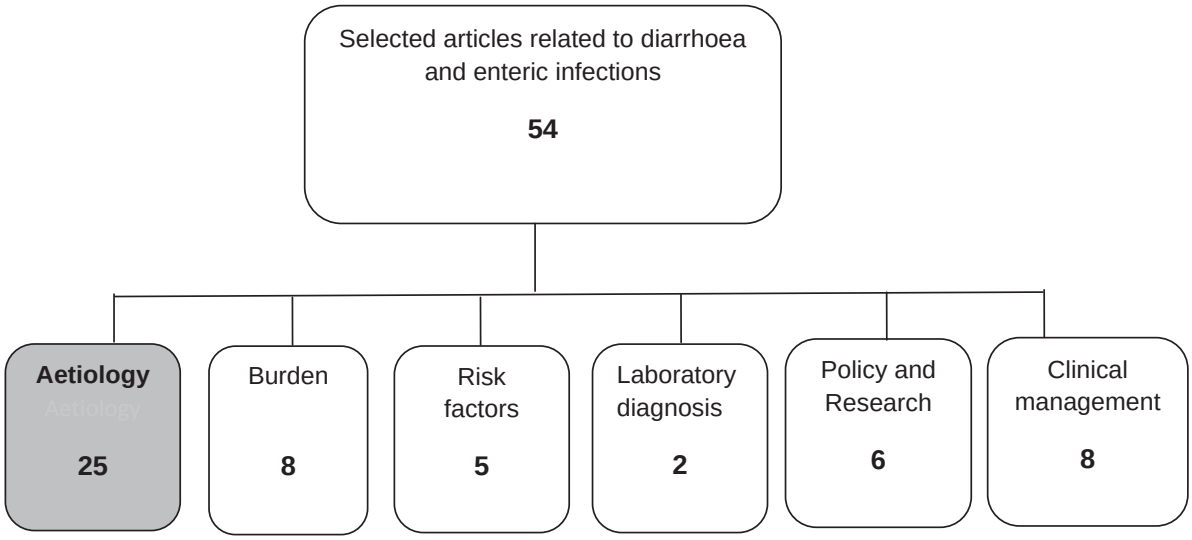

Figure 1. Categorization of selected articles retrieved from medical subject heading (MeSH) searches and included in analysis.

time that typhoid had become endemic in the highlands (20,21). This trend was also reflected in Larsen's review of typhoid data from Enga Province from 1986 to 1991 (22). Discharge rates in the province from provincial and district-level health care facilities where typhoid was the primary diagnosis rose from 5.5% in 1981 to 18.1% in 1991, reflecting the rise in the attack rate from 46.9 per 100,000 to 122.2 per 100,000. There are insufficient data published from centres outside of the highlands to determine the extent of typhoid fever elsewhere in the country, although it is known to have occurred in Port Moresby and other coastal towns (20). Moreover, the National Health Plan presents national data on typhoid, in the form of monthly admissions to health facilities (1), but they are difficult to interpret. What can be deduced from the National Health Plan is that there seems to be a steady decline in national typhoid admission rates between 2001 and 2009, although the burden in different regions is unclear (1). The most recent data on typhoid come from Siba et al. (23) from research undertaken in 2011. While the primary aim of their research was to evaluate typhoid diagnostic tests, the 9.4% typhoid positivity (by either blood culture or polymerase chain reaction (PCR)) represents not only the most recent published work on typhoid in PNG but also an estimate of prevalence among patients clinically suspected of typhoid in Goroka (23). There is certainly a need for country-wide prevalence and incidence data that are based on laboratory diagnosis of typhoid to accurately elucidate the extent of the typhoid problem in PNG.

Only two studies provide data specifically on the contribution of *Salmonella* spp. infection to child morbidity and mortality in PNG. Howard et al. (6) reported that among children in Goroka *Salmonella* spp. were isolated from 4.1% of patients with diarrhoea compared with 0.5% of controls. Although not all tests were done for study participants, rotavirus (23.3%), *Shigella* spp. (13.1%), *Campylobacter* spp. (12.2%), *Cryptosporidium parvum* (10.1%) and enteropathogenic *Escherichia coli* (EPEC) (8.2%) were more commonly isolated among paediatric diarrhoea cases than *Salmonella* spp. Furthermore, the contribution of *Salmonella* spp. to paediatric mortality may not be as great as other aetiological agents. In reviewing the causes of death among children at Goroka Hospital between 1998 and 2000, Duke et al. (5) found that only three children (0.8%) had Widal titres exceeding 360 (although their blood culture was negative) and clinical signs of typhoid. These data suggest that in young children in PNG typhoid may not be as important as other enteric infections such as rotavirus. However, the research studies published by Duke et al. (5) and Howard et al. (6) were conducted more than 10 and 20 years ago respectively, and thus it is possible that the pattern of diarrhoea aetiology in children in PNG may have changed.

In addition to endemic typhoid, outbreaks were also reported in the literature (24,25), although the distinction between sporadic cases and endemicity is not always clear. Richens (25) reported an outbreak at Goroka Hospital between 1984 and 1990 that had an estimated case fatality rate of 10-15%. Outbreaks are not limited to the typhoid-endemic region of the highlands, with a typhoid outbreak reported at two settlements within the National Capital District (NCD) (24). This outbreak affected 10 of 31 residents from one settlement and 10 of 50 inhabitants of three households from another settlement. The outbreak investigation in NCD indicated that all affected households were related by either blood or marriage and where the sharing of living quarters and meals was frequent. These examples illustrate the potential for high transmission given the PNG context of poor hygiene and sanitation, poor access to safe water and the common practice of shared living quarters and meals (24,26). Work done by Passey et al. (21) highlighted the minor role that chronic carriers play in transmission of the causative agent, *S. enterica* serovar Typhi. Thus transmission in PNG is primarily through contact with sick patients, with food being the most probable vehicle of transmission (21,27,28).

Understanding the molecular epidemiology of *S. enterica* Typhi is important given the reported endemicity of typhoid in PNG and the frequency of sporadic outbreaks. Molecular characterization can provide information on epidemiological relationships between isolates, particularly when investigating the source and movement of an outbreak. Our knowledge of *S. enterica* Typhi strain diversity in PNG has evolved as more powerful discriminatory methods of characterization have become available. We found five studies that have characterized *S. enterica* Typhi isolates from PNG and investigated diversity

at the molecular level (29-33). These studies provided information on strain types by geographical distribution, changes in diversity over time and the relationship between strain type and virulence.

Characterization of strain types was carried out on isolates collected during the 1990s, when high attack rates of typhoid were reported in the highlands. Initially, pulse-field gel electrophoresis (PFGE) analysis comparing profiles of isolates collected from 1992 to 1994 and those collected from 1997 to 1999 indicated that variability among isolates had increased over that period of time (32,33). Ribotyping of isolates collected between 1985 and 1996 demonstrated that there were strains endemic to PNG (ribotypes 1, 2 and 3), having been isolated consistently for over a decade (30). Several strains (ribotypes 4-9, 16 and 17) seemed unique to PNG and one strain was common to Malaysia and Thailand (ribotype 3) (30). Subsequently, amplified fragment length polymorphism (AFLP) fingerprinting was able to demonstrate a higher degree of discriminative power when isolates previously characterized by PFGE and ribotyping were re-analysed (31). AFLP was able to detect diverse genotypes within strains that were previously shown to have the same PFGE or ribotype profile (31). These AFLP data are now over a decade old and if typhoid incidence has decreased in the last decade, as suggested by data from the National Health Plan (1), it would be interesting to determine which strain types continue to persist.

Characterization studies also enable the determination of association between strain types, virulence and clinical outcomes. Thong et al. reported that isolates from fatal cases of typhoid had the same PFGE profile while those isolated from non-fatal cases had variable profiles (32,33). However, a connection could not be deduced between genotype and virulence with the increased discrimination afforded by AFLP (31). Furthermore, Baddam et al. (29) used whole genome sequencing to show that two isolates – one isolated from a fatal typhoid case and the other from a non-fatal typhoid case – possessed all major virulence factors and genes relevant to toxicity and immune evasion. This suggests that clinical outcome is not influenced by virulence potential alone but that other factors may be involved such as late presentation and poor compliance with treatment (27).

Diagnoses that utilize both clinical and laboratory evidence enable prompt and effective patient care. The diagnosis of typhoid based solely on clinical symptoms is particularly challenging since other common diseases in PNG, such as malaria and diarrhoeal diseases, share similar signs and symptoms. In many cases treatment for typhoid is administered based on a clinical diagnosis and no laboratory confirmation, leading to the population's over-exposure to antibiotics. Although almost no chloramphenicol resistance was reported among *S. enterica* Typhi in PNG almost two decades ago (27), continued antimicrobial surveillance of *S. enterica* Typhi is warranted since patterns of antimicrobial susceptibility can change in a short period (34). This is important in a setting where overtreatment with and indiscriminant use of antibiotics are common.

The need for a robust, rapid and simple test for typhoid in PNG has been echoed since typhoid's emergence in PNG (27). Clegg (27), in reviewing the diagnostic tests for typhoid available during the mid-1990s, stated that for a test to be of value in PNG it should be rapid, sensitive, specific and simple to use in rural settings. Currently the gold standard for typhoid laboratory diagnosis is bone marrow culture but due to the procedure's invasiveness and technical difficulty, blood culture is commonly preferred for routine laboratory diagnosis. Unfortunately, in PNG only a few laboratories have the capacity to perform culture. While the Widal antibody test remains the primary method of laboratory diagnosis of typhoid in PNG, it has many limitations including its lack of specificity in typhoid-endemic areas, where the population may have high levels of background antibodies due to previous exposure to typhoid. The cut-off titre for the Widal test was last evaluated over two decades ago, so a multicentre evaluation of cut-off titre is warranted if the test continues to be used in PNG (35). Until a rapid, robust and simple-to-use diagnostic test is available, PNG will continue to face challenges in accurately diagnosing patients, not only for the purpose of care and treatment but also for surveillance and understanding typhoid epidemiology in the country.

Recently Siba et al. (23) evaluated two commercially available rapid diagnostic tests (Tubex and TyphiDot), a prototype (TyphiRapid TR-02) and the Widal test in Goroka against a

composite reference standard of blood culture and PCR. The two commercially available kits and the Widal test demonstrated low sensitivity against the composite reference although their specificity was acceptable. The TR-02 prototype showed the most promising results, with a sensitivity and specificity of 89.4% and 85.0% respectively. There was marginal improvement in sensitivity and specificity of all tests used on patients with axillary temperatures ≥38°C. Siba et al. (23) also demonstrated that the current Widal cut-off titre of 160 resulted in a test with poor sensitivity but very high specificity. It may be that typhoid fever is less common in this setting now than previously and thus there may be lower levels of background antibodies in healthy individuals. In such a case the sensitivity of the Widal test may be improved by the lowering of the cut-off titre, although some decrease in specificity may also result. As mentioned previously, an evaluation of cut-off titres for the Widal test is warranted, particularly in gauging antibody levels in asymptomatic patients throughout the country. Only then, and in conjunction with antibody titres in typhoid fever patients, can an optimal cut-off titre be determined for the Widal test. In the absence of a non-expensive and robust test that can be used effectively in typhoid-endemic areas the task of elucidating the true burden of typhoid within PNG remains an elusive pursuit.

Shigellosis

The four species of the genus *Shigella* (*S. flexneri, S. dysenteriae, S. boydii* and *S. sonnei*) cause shigellosis, an acute invasive enteric infection that manifests as diarrhoea that is commonly bloody, with *S. flexneri* being the leading cause of endemic shigellosis in developing settings (36). Data collected from Port Moresby General Hospital between 2000 and 2009 show that *Shigella* spp. were isolated in 4% of stool samples that underwent culture and of these (n = 136) over 90% were *S. flexneri* (8). Furthermore, 48% of *Shigella* spp. isolated were from children under five years of age (8). Howard (37) found that *Shigella* was the second most common aetiology detected in children with diarrhoea (13.1%) in Goroka after rotavirus. *Shigella* was also more commonly isolated from children at least 12 months of age, with the highest proportion seen in children between the ages of 24 and 36 months (27.0%) (6). Therefore *Shigella*, most notably *S. flexneri*, is a common cause of diarrhoea in PNG, particularly in children under five years of age.

A characteristic clinical feature of shigellosis is diarrhoea with the presence of blood and sometimes pus (36). Howard et al. (6) reported that 70% of children from whom *Shigella* was isolated had blood in their stool, 52% had pus in their stool and 69% had diarrhoea accompanied by fever. A hospital-based study of children presenting with persistent diarrhoea (4) reported that although less than 2% of children had blood in the stool as a presenting symptom, a review of clinical records indicated that 12% of cases had experienced bloody diarrhoea. Similarly, another community-based study investigating diarrhoea morbidity in children from the highlands found that 5% of diarrhoea cases reported blood in the stool. As in other settings, the work of Howard et al. (6) demonstrated that blood in the stool is highly suggestive of *Shigella* spp. infection and that shigellosis is probably the cause of up to 10% of diarrhoea cases in children in PNG.

Cholera

Cholera had not been reported in PNG until a nation-wide outbreak occurred between 2009 and 2011 (38). A total of five articles pertained to this recent cholera outbreak (2009-2011) in PNG. Two articles reported specifically on aetiology, including molecular characterization of *Vibrio cholerae* strains isolated during the outbreak (10,11). Another two articles discussed risk factors associated with cholera transmission in PNG (38,39) and one article described the lack of laboratory capacity as a major handicap in PNG's response to the recent outbreak (40). Published data from the recent nation-wide outbreak highlight the strong potential for future outbreaks, given poor access to clean and safe water coupled with poor hygiene and sanitation practices, as well as PNG's unpreparedness to respond to outbreaks, particularly in remote and rural areas.

Horwood and Greenhill (38) reported that by the middle of 2011 approximately 15,500 cases and 500 deaths had resulted from the outbreak, giving a CFR of over 3%. The high overall CFR was primarily attributed to the numerous challenges posed in responding to and managing the outbreak in remote and rural areas in PNG (40). In contrast the well-serviced National Capital District had a CFR

of 0.1% (38). The inaccessibility of the rural majority coupled with a lack of health services resulted in a general unpreparedness for the outbreak as attested by the high CFR (38). The recent outbreak has certainly highlighted the detrimental results of an ongoing decline of services to the rural majority.

All *V. cholerae* strains isolated during the outbreak were initially categorized as O1 El Tor Ogawa through standard bacteriological methods and later confirmed by polymerase chain reaction. Molecular characterization was also conducted to determine the origin of outbreak strains using multi-locus sequence typing (MLST) and variable number tandem repeats (VNTR). VNTR demonstrated that PNG strains were most closely related to strains isolated in Vietnam in 1995 and 2002-2004 while MLST indicated that strains from Bangladesh were closely related to PNG strains. VNTR is known to have a greater discriminatory power than MLST; however, a direct comparison was not possible because MLST data were not available for strains from Vietnam. The homogeneity of outbreak strains suggests a recent introduction to PNG from South-East Asia (10).

The potential for future cholera outbreaks in PNG is high since sustained and widespread transmission of the pathogen during the recent outbreak may have established an environmental reservoir (38). Such a reservoir coupled with concentrated populations, poor standards of sanitation and hygiene, and lack of safe drinking water, all of which are common in PNG communities, provides a strong potential for future cholera outbreaks and ease of sustained transmission. Furthermore, these factors provide the foundation for PNG to become a cholera-endemic country (38,39).

Rotavirus

Infection with rotavirus is an important cause of diarrhoea throughout the world, primarily in children. Its role in childhood diarrhoea in PNG has been previously described (41) but in this review only two articles relating to the prevalence and molecular characterization of rotavirus were found (6,9).

Howard et al. (6) detected rotavirus by ELISA in 23.4% of 903 children with diarrhoea presenting at Goroka Hospital over a five-year period. Horwood et al. (9) found a comparable proportion (31.2%) in their study of children with gastroenteritis presenting at the same hospital more than two decades later. In their studies both Howard et al. (6) and Horwood et al. (9) found that the majority of children infected with rotavirus were under the age of two years: 96.2% and 90.9% respectively. In the study of Horwood et al. (9), 2.4% of cases resulted in death. Both studies were conducted at the same hospital in the highlands and thus these data may not be representative of rotavirus infection in the rest of PNG; however, the fact that rotavirus may be responsible for at least a quarter of hospitalized cases of diarrhoea in young children in the highlands cannot be ignored.

Diarrhoea caused by rotavirus infection is characteristically watery and often associated with vomiting. Howard et al. (6) found that 73.3% of diarrhoea cases where rotavirus infection was detected were accompanied by vomiting. Han et al. (4) conducted a study at PMGH on persistent and non-persistent diarrhoea in children and, although no aetiology was reported, there was up to a 12-fold increase in diarrhoea accompanied with vomiting during the drier months from May to July. In regions where seasons are more pronounced, rotavirus infection is most common in drier, cooler months. Horwood et al. (9) found that rotavirus infection in children peaked between May and July, a period that is typically dry in Goroka. While PNG does not experience pronounced seasons, the data available suggest that there may be seasonality to rotavirus transmission.

Since the data available suggest that rotavirus infection contributes to a considerable proportion of diarrhoea cases in young children in PNG, the introduction of a rotavirus vaccine may be a possibility in the near future. Data on rotavirus strain types in circulation is necessary for determining if current vaccines will be effective in PNG. Horwood et al. (9) conducted molecular characterization of rotavirus detected between 2008 and 2010 from patients in Goroka and found that the common global strain types of G1P[8], G3P[8] and G2P[4], which are covered by vaccines that are currently available, were represented in the following proportions in PNG: 50.0%, 23.0% and 8.2%, respectively. It is vital that surveillance activities accompany the introduction of a vaccine program in order to monitor the vaccine's impact on strain types in addition to monitoring emerging strain types not covered by vaccines that are currently

available, such as G9 (1.2%) and G12 (6.1%), which are already present in PNG.

Pigbel

Pigbel, or enteritis necroticans, is an often fatal food poisoning caused by a β-toxin of *Clostridium perfringens* type C (42). A distinguishing clinical feature of pigbel is acute abdominal pain accompanied by other symptoms such as bloody diarrhoea, vomiting blood and upper abdominal distension (15). In the 1960s and 1970s pigbel was the most common cause of death in children above the age of one year in the PNG highlands but fortunately the introduction of a vaccine in the 1980s virtually eradicated the disease (42,43). Only one article pertaining to pigbel was included in this review (15).

Poka and Duke (15) conducted a study (2001-2002) to elucidate the occurrence and magnitude of pigbel in the PNG highlands in order to inform vaccine policy decisions. Of the 119 children aged between 1 and 12 years who presented with acute abdomen in the 12-month survey period, 9.2% were classified by the case definition as pigbel while another 6.7% were deemed probable cases. The CFR in the study was 18% and it was estimated that pigbel accounted for 9% to 16% of cases of acute abdomen, less than dysentery (33%) and typhoid (21%). This study found that cases of pigbel seemed to occur in clusters, suggesting that widespread reintroduction of the pigbel vaccine was not warranted. However, continued surveillance remains important, particularly in previously endemic areas. Pigbel certainly should be considered in cases of acute abdomen when present with other symptoms indicative of the disease, particularly in highlands children.

Other bacterial and parasitic agents

Data on the contribution of other bacterial and parasitic enteric pathogens to the burden of diarrhoea in PNG is limited, with the exception of the study by Howard et al. (6). Their study found that *Campylobacter* spp. (12%) and EPEC (8%) were commonly isolated in children with diarrhoea in Goroka. These proportions were only slightly less than *Shigella* spp. (13.1%) and greater than *Salmonella* spp. (4.1%) (6). Similarly, important parasites such as *Entamoeba histolytica* (4.1%) and *Cryptosporidium parvum* (10.2%) were reported only by Howard et al. (6). The study reported by Howard et al. (6) is certainly the most comprehensive work to date on diarrhoea aetiology in children; however, there remains little known about diarrhoea aetiology throughout the rest of the country and also within adult populations.

One study was conducted in Eastern Highlands Province to investigate the burden of *Serpulina pilosicoli*, an intestinal spirochaete that commonly causes porcine intestinal spirochaetosis (14). *S. pilosicoli* can also infect a range of hosts including humans, where it can cause chronic diarrhoea and rectal bleeding. In their initial survey Trott et al. (14) found an overall prevalence of 22.8% in participants from five villages surveyed. In the first survey, infection with *S. pilosicoli* was not associated with diarrhoea, age or sex. Despite treatment with tinidazole, six weeks later Trott et al. found that 93.6% of individuals found to be infected in the initial survey were infected again (14). It was also found that detection of *S. pilosicoli* was more commonly associated with watery stools than normal stools in the second survey. *S. pilosicoli* was not detected in any of the village pigs surveyed but it was detected in 4 of 76 village dogs, suggesting that transmission might have occurred between humans and animals. The practice of living in close proximity to animals, such as pigs, is common in rural areas in PNG and thus provides great potential for transmission of enteric pathogens that infect both humans and animals.

Two papers reported on infection with intestinal helminths, although not in direct association with diarrhoea. King and Mascie-Taylor (12) investigated the prevalence of intestinal helminths in children from Kanabea in Gulf Province and found that 68% of children were infected with one or more of either *Ascaris lumbricoides*, *Necator americanus* (hookworm) or *Strongyloides*. While they did not collect data on diarrhoea they did report that the people in this area were prone to poor nutrition, malaria, respiratory infections, diarrhoea and anaemia. This study reported two variables to be strongly associated with helminth infection in children: living in a home with six or more occupants, and having an uneducated mother. Pritchard (13) reported the prevalence of hookworm to be nearly 100% on Karkar Island, Madang Province. During this study an intervention of pyrantel pamoate was administered but after two years the prevalence of hookworm infection had

returned to pre-treatment levels. Pritchard (13) highlighted the need for improved sanitation and hygiene as measures to break the transmission cycle and reduce the burden of hookworm infection in this population.

Diarrhoea associated with other infections

Diarrhoea is also common, although perhaps not the primary presentation, in other important infections in PNG. This review found four papers that reported diarrhoea as one important presenting symptom of other infections. Benjamin and Dramoi (16) reported on a measles outbreak in Port Moresby in a six-month period in 2001. A total of 492 measles cases were reported at PMGH, of which 72% were admitted to the Paediatric Ward. In admitted patients, 44% presented with diarrhoea and pneumonia, 33% had pneumonia but not diarrhoea while 15% presented with diarrhoea alone. Three papers were related to HIV. Friesen (18) and Seaton et al. (19) described the clinical features of HIV infection and AIDS in children and adults respectively, in which persistent diarrhoea was featured. Allison et al. (17) conducted a study at PMGH looking at predictors of HIV testing in children admitted to the Paediatric Ward. This study found that children under the age of 18 months who had been admitted for more than seven days with diarrhoea, malnutrition or oral candidiasis were more likely to be tested than children without these symptoms. 27% of the 215 children that had an HIV test were positive. The presentation of diarrhoea among other symptoms in important diseases in PNG is common. Furthermore, its treatment and management is an important part in preventing further deterioration of the patient. This again raises the importance of diagnosing the disease aetiology to allow prompt and effective treatment of patients.

Conclusion

This review of data published over the last 18 years on enteric pathogens that commonly cause diarrhoea in PNG suggests that diarrhoeal diseases present an ongoing public health challenge within the country. During this period, only 25 published articles were found that were directly related to the aetiology of diarrhoea. The amount of PNG data published on a particular aetiology may not necessarily reflect its contribution to the diarrhoeal disease burden within this setting. This finding ultimately reflects the limited laboratory capacity of most centres in PNG to provide routine laboratory diagnosis of diarrhoea. Many of the diagnostic methods presented in the studies reviewed would be confined to research laboratories and certainly would not be available for routine laboratory diagnosis at health care facilities. Undoubtedly, this limited application of contemporary diagnostic methods negatively affects the quality of epidemiological and aetiological data pertaining to diarrhoea and our ability to detect and monitor outbreaks.

Many of the studies included in this review of diarrhoea aetiology were conducted on populations within the highlands of PNG. This is an artifact of the location of the country's premier health research facility, the PNG Institute of Medical Research, in Goroka, Eastern Highlands Province. Thus a significant gap in what we know about diarrhoea aetiology in PNG relates to patterns of aetiology in other parts of the country.

In PNG, poor sanitation and hygiene practices and lack of safe drinking water perpetuate the faecal-to-oral transmission necessary for the persistence of enteric pathogens. Unless these issues are adequately dealt with through education and awareness and the provision of infrastructure and services to enable behaviour change, diarrhoea will continue to be a leading cause of morbidity and mortality in PNG.

In 1986, an editorial written by Howard (37) in this Journal listed six objectives which, if addressed, would provide more precise epidemiological information and informed interpretations to health planners and those responsible for implementing and evaluating interventions aimed at reducing the burden of diarrhoeal diseases. The first four of these objectives encompass the collection of quality country-wide incidence data on diarrhoeal disease, the identification of common aetiology at health care facilities as well as at the community level, and determining the transmission dynamics of common diarrhoea-causing pathogens. Published data on diarrhoea aetiology over the last two decades have taken some steps toward meeting these objectives, but there is scope for a more systematic research effort toward better understanding the aetiology of diarrhoea in PNG. This will help guide measures aimed at reducing the burden of disease caused by diarrhoea in the country.

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