Current Issues of Gastroenterology in Indonesia

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ABSTRAK

Indonesia merupakan salah satu negara berkembang dengan penduduk terbanyak di dunia. Sama seperti negara berkembang lainnya, Indonesia mempunyai angka insidens penyakit gastroenterologi yang tinggi dan sebagian besar disebabkan oleh infeksi. Beberapa tahun terakhir, Indonesia juga mengalami peningkatan penyakit gastroenterologi non infeksi seperti inflammatory bowel disease, gastroesophageal reflux disease, dan kanker kolorektal. Saat ini berkat kerjasama lintas sektor, telah terjadi perkembangan pesat dari modalitas diagnostic dan terapeutik. Hal ini bertujuan untuk meningkatkan kesehatan pencernaan di Indonesia.

Kata kunci: *penyakit gastroenterologi, Indonesia, negara berkembang, prevalensi, layanan kesehatan.*

ABSTRACT

Indonesia is one of the most populous developing countries in the world. Similar with other developing countries, Indonesia has been suffered from the high incidence of gastroenterology diseases that mainly due to infection. In the recent years, Indonesia had also increased number of non-infectious gastroenterology diseases cases such as inflammatory bowel disease, gastroesophageal reflux disease, and colorectal cancer. Nevertheless, the developments of diagnostic and therapeutic modality along with the cooperation between sectors have undergone rapid progress as an effort in improving digestive health in Indonesia.

Keywords: *gastroenterology disease, Indonesia, developing country, prevalence, healthcare.*

INTRODUCTION

Indonesia is one of the largest developing country in the world with total population of 255 million people and population density of 134 people/km^2.[1] As other developing countries, Indonesia healthcare problems are related with poverty especially in rural area (62.76%) and low sanitation level due to lack of clean-drinking water access, hand and food hygiene awareness, also due to slum areas.[2-4]

In the past few years, Indonesia has undergone significant improvement in the healthcare and economics field. National Survey in 2015 showed the national percentage of households with clean drinking water access reached 70.97% and the number of hand hygiene awareness reached 65.83%.[2] Access to adequate and sustainable sanitation in 2015 reached the national coverage of 62.14%; however in rural areas the coverage was still less than 50%.[5] These challenges contribute to the high incidence of gastrointestinal infections that lead to increased

morbidity and mortality. Indonesia is also faced with increasing cases of gastrointestinal cancers that are often associated with changes in diet and lifestyle; therefore increasing early detection screening and cancer awareness are required for healthcare provider and community.

GASTROENTEROLOGY DISEASES IN INDONESIA

Gastroenterology diseases still remain major health problems in Indonesia. National Survey in 2010 showed that diarrhea, gastroenteritis, and colitis were ranked fifth in the list of top ten leading diseases in outpatient setting, while dyspepsia ranked sixth.[6] (**Table 1**) According to National Hospitalization Data, diarrhea was the most prevalent disease in inpatient setting with case fatality rate (CFR) of 1.79%, then followed by typhoid fever in third place, and dyspepsia in fifth place.[6] (**Table 2**)

In 2007, the prevalence of diarrhea in Indonesia were 9% and become the most common cause of death among babies (31.4%), also ranked fourth leading cause of death among all ages (13.2%). Decreased diarrhea prevalence was reported in 2013 which declined to 7% among all ages.[7] Data in 2015 reported 18 outbreak cases of diarrhea were occurred

Table 1. Pattern of 10 most frequent diseases in the outpatient clinic In Indonesian Hospitalas year 2010[6]

Type of diseases	New cases	All cases
Acute upper respiratory tract infection	291 356	433 354
Multiple body injury trauma	127 076	168 768
Skin and subcutaneous diseases	122 076	192 414
Refractive and accomodative abnormalities	111 513	143 404
Diarrhea, gastroenteritis caused by specific infection (infective colitis)	105 279	141 556
Dyspepsia	88 599	163 428
Pulpa and periapical diseases	86 421	163 211
Essential hypertension (primary)	80 615	277 846
Conjunctivitis and other abnormalities	68 026	87 513
Ear and mastoid processus diseases	61 438	99 663

Table 2. Pattern of 10 most frequent diseases in the inpatient ward in Indonesian Hospital year 2010[6]

Type of disease	Patient discharge	Patient death	CFR (%)
Diarrhea, gastroenteritis by other specific infection (infective colitis)	71 889	1 289	1.79
Dengue hemorrhagic fever	59 115	325	0.55
Typhoid and paratyphoid	41 081	274	0.67
Fever	40 636	276	0.68
Pregnancy and other delivery complications	24 716	166	0.67

in Indonesia with CFR 2.47%. National morbidity rate of diarrhea reached 214/1,000 with estimation of 5,405,235 diarrhea cases were occurred in 2015, in which 74.3% of cases were managed in health care facility.[2] The etiology of acute diarrhea in Indonesia includes virus, bacteria, and parasites (**Table 3**). The bacterial pathogens of acute diarrhea in Indonesia are *Vibrio cholerae 01, Vibrio cholerae 0139, Vibrio parahaemolyticus, Escherichia coli*, *Campylobacter jejuni, Salmonella sp., Clostridium difficile, Yersinia enterocoiltica* and *Shigella sp*.[8] Viral agents causing diarrhea are Rotavirus, Norovirus (Calcivirus), Adenovirus, Astrovirus, Cytomegalovirus, and Coronavirus.[8] While the parasites include protozoa (*Giardia lamblia*, Cryptosporodium) and helminthes (*Strongyloides sp*.).[8] Report from one of referral hospital in Jakarta, found that most cases of acute diarrhea were caused by *E. coli* pathogenic (38.29%), followed by *V. cholera* Ogawa (18.29%), and *Aeromonas, sp*. (14.29%).[9] Simanjuntak et al.[10] reported the incidence of Cholera cases caused by *Vibrio cholera* Ogawa from 1993 – 1999 ranged from 6 % to 72%; with the highest incidence in Aceh, and the lowest incidence was in Jakarta. Surveillance study in Indonesia conducted by Oyofo et al.[11] found that among 6760 acute diarrhea cases, 9% of the patient stools were positive for bacteria. The most prevalent pathogen isolated was Shigella flexneri (39%), followed by Sal*monella sp.* (26%), and *Vibrio sp.* (26%). High prevalence number of acute diarrhea in Indonesia is closely related with low level of environment sanitation, personal and food hygiene awareness, access to

Table 3. Causative agents of acute diarrhea in Indonesia[8]

Bacteria	Viruses	Parasites
Vibrio cholerae O1	Rotavirus	Protozoan
V. parahaemolyticus	*Norovirus (Callcivirus)*	Microsporidia
Escherichia coli	*Adenovirus (serot.40/41)*	*Encephalitozoan bleneusi*
Plesiomonas	*Astovirus*	*Enterocytozoan intestinales*
Aeromonas	*Cytomegalovirus*	*Giardia intestinalis*
Bacteroides fragilis	*Coronavirus*	*Cryptosporidium hominis*
Campylobacter jejuni		*Entamoeba histolytica*
C. coli		*Isospora belli*
Cupsaliensis nontyphoidal		*Cyclospora cayetanenesis*
Salmonella		*Dientamoeba fragillis*
Clostridium difficile		*Blastocystis hominis*
Yersinia enterocolitica		
Y. pseudotuberculosis		Helminths
Shigella species		*Strongyloides stercoralis*
		Anglostrongylus costakensis
		Schistosoma mansoni

clean drinking water, level of education, social status, and high number of malnutrition, poverty, population density, and flood events.[12]

Regarding chronic diarrhea in Indonesia, data from Division of Gastroenterology Universitas Indonesia showed prevalence rate of 15% among all colonoscopy procedures performed.[13] Simadibrata et al.[13] reported that the most common etiology of chronic diarrhea in Indonesia was due to infection (48.3%) which caused by *Candida albicans* (48.6%), bacterial (pathogenic *E.coli*, etc.), parasites (*Entamoeba histolytica, helminthes,* etc.) (**Table 4 and 5**). While, the non-infectious causes of chronic diarrhea (33.3%) were carbohydrate maldigestion (62.6%), colorectal carcinoma (14%), Chron's disease (11.2%), radiation colitis, enteropathy, and others.[14] (**Table 6**)

Dyspepsia ranked sixth among the most common complaints in outpatients setting in Indonesian Hospital.[6] Study in Indonesia found that among 550 patients with dyspepsia who underwent endoscopic examination were found gastritis (44.7%), duodenitis (6.5%), peptic ulcer (3.6%), duodenal ulcer (8.2%) and gastric tumor

Table 4. Etiologies of chronic diarrhea[14]

Pattern of chronic diarrhea	n (%)
Chronic Infective	100 (48.3)
Mixed chronic Infective and non-infective	38 (18.4)
Chronic non-infective	69 (33.3)
Total	207 (100.0)

Table 5. Etiologies in patients with chronic infective diarrhea[14]

Microorganisms	n (%)
Candida albicans	67 (48.6)
Pathogenic E.coli	48 (34.8)
Blastocystis hominis	9 (6.5)
Giardia lamblia	5 (3.6)
Entamoeba histolytica	5 (3.6)
Ascaris lumbicoides	5 (3.6)
Trichuris trichiura	5 (3.6)
Aerobacter aerogens	5 (3.6)
Mycobacterium tuberculosis	5 (3.6)
Klebsiella ocoma	5 (3.6)
Klebsiella oxytoca	5 (3.6)
Salmonella paratyphi	4 (2.9)
Klebsiella pneumonia	4 (2.9)
Alcaligens dizpar	4 (2.9)
Geotrichum	2 (1.5)
Pseudomonas spp.	1 (0.7)
Yersinia entercolytica	1 (0.7)
Clostridium perferingens	1 (0.7)
Shigella flexneri	1 (0.7)
Entamoeba coli	1 (0.7)
Shigella zoonotic	1 (0.7)

Table 6. Etiology in patients with chronic non-infective diarrhea[14]

Causes	n (%)
Carbohydrate maldigestion	67 (62.6)
Colorectal carcinoma	15 (14.0)
Chron's disease	12 (11.2)
Colorectal polyp	11 (10.3)
Ulcerative Colitis	10 (9.3)
Irritable Bowel Syndrome	9 (8.4)
Portal hypertensive enteropathy	7 (6.5)
Colorectal diverticulosis	6 (5.6)
Carbohydrate fat maldigestion	6 (5.6)
Radiation colitis	5 (4.7)
Lactose intolerance	5 (4.7)
Fat maldigestion	4 (3.7)
Jejunal villeus atrophy due to celiac disease	3 (2.8)
Lymphoma	3 (2.8)
NSAID enteropathy	2 (1.9)
Prostigmin therapy	1 (0.9)
Food allergy	1 (0.9)
Amyloidosis	1 (0.9)
Eosinophilic duodeno-jejuno-ileo-colitis	1 (0.9)
Lymphocytic colitis	1 (0.9)
Jejunal carcinoma	1 (0.9)
Unknown	5 (4.7)

(0.2%).[15] Several studies regarding *H. pylori* prevalence in Indonesia had been conducted since 1998 to 2015, which showed prevalence between 0 to 68%, it depends on the location of study and diagnostic testing methods being used.[16] In 2015, Syam et al.[16] conducted prevalence study of *H. pylori* infection in five islands in Indonesia, which found prevalence of 22.1% (59/267), with the largest group was aged 50-59 years (29.8%).[16] This finding suggested that the prevalence of *H.pylori* infection in Indonesia is lower than other countries in Asia and several countries in the world.[17] The prevalence of *H.pylori* in Indonesia shows variation between ethnic groups, with the highest was found among Papuan (42.9%), Batak (40.0%), Buginese (36.7%), and Chinese (13%).[16]

H. pylori antibiotic resistance data reported by Miftahussurur et al.[18] in 2016 stated that among 849 dyspeptic patients who underwent endoscopy in 11 cities in Indonesia, there were total of 77 *H. pylori* strains with 28 strains (36.4%) were sensitive of all antibiotics, and they also found low resistance to clarithromycin (9.1%), amoxicillin (5.2%), tetracycline (2.6%). In contrast, high resistance rates to metronidazole (46.7%) and levofloxacin (31.2%) were identified. There were differences in *H. pylori* antibiotic susceptibility between cities in Indonesia, such as Clarithromycin resistance was found ranged between 0-21.4% and resistance to metronidazole ranged from 20 to 88.9%.[18] Previous study in 2006 showed that among 72 *H. pylori* specimens in Jakarta were found resistant to metronidazole (100%), clarithromycin (27.8%), amoxicillin (19.4%), dan levofloxacin (1.4%).[19] Therefore it can be concluded that knowledge regarding local data of *H. pylori* antimicrobial susceptibility in Indonesia are necessary to administer the most effective eradication regiments.

The prevalence of gastroesophageal reflux disease (GERD) in Indonesia is increasing recently; study from Cipto Mangunkusumo National Referral Hospital found increased prevalence from 5.7% in 1997 to 25.18% in 2002.[20] Another GERD prevalence study which involved 515 general practitioners in Indonesia was found prevalence of 27.4%, with risk factors such as older than 50 years old, obesity, and smoking habit.[21]

Beside the vast majority of gastrointestinal tropic-infection diseases problem, Indonesia also has increased gastrointestinal tumor prevalence which warranted further action. According to GLOBOCAN World Health Organization 2012, colorectal cancer ranked fifth as the most prevalent cancer in Indonesia, followed by hepatoma in the seventh rank, gastric cancer in fourteenth place, and pancreatic cancer in the fifteenth (**Figure 1**).[22] Among group of male, colorectal cancer is the second most prevalent cancer in Indonesia (age standardized rate [ASR] per 100,000: 15.9). The prevalence of colorectal cancer in Indonesia for both sexes reached 9.3% with ASR 12.8 per 100,000 and mortality rate of 9.5% (ASR: 8.6).[22] Annual report from Indonesian Society of Anatomic Pathology in 1995 stated that more than 30% of colorectal cancer were found in patients aged below 40 years old and generally diagnosed at 45-50 years old.[23] This finding was in contrast with report from American Cancer Society that up to 90%

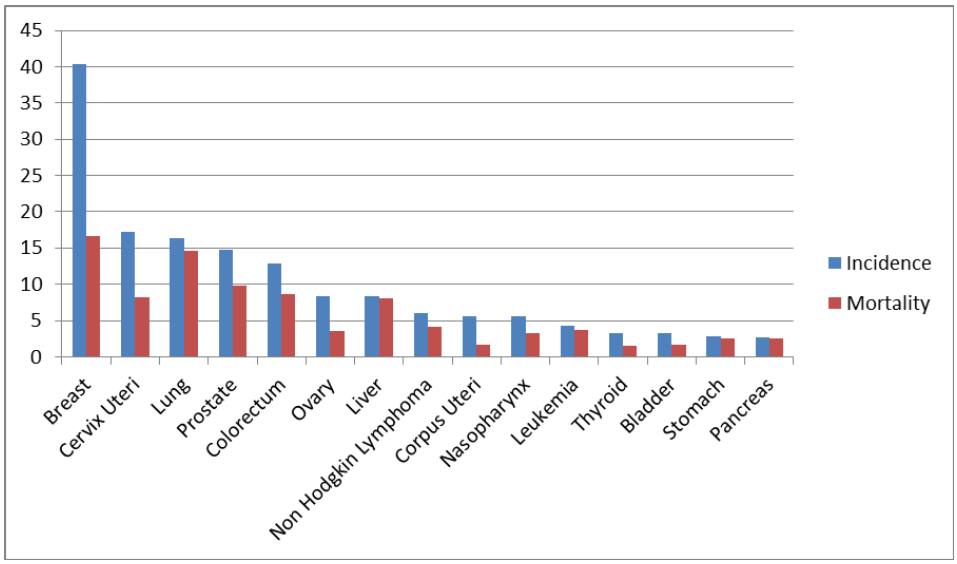

Figure 1. Estimated age-standardised incidence and mortality rates in Indonesia, Both Sexes.[22] (ASR rate per 100,000)

of new cases and 93% death cases occurred in American citizens older than 50 years old.[24] Another report from one of digestive centers in Indonesian private hospital showed that among 1695 patients whom undergone colonoscopy; 29.8% of them were found to have polyp or colon masses, and neoplastic lesion was found in 16.1% patients with adenoma (11.3%), in situ carcinoma (0.6%), and carcinoma (4.2%). Polyp or masses were more commonly found in male (25% vs. 23.9%; $p<0.001$) and patients aged more than 50 years old (39.6% vs. 16.6%; $p<0.001$).[25] Increasing prevalence of colorectal cancer in Indonesia may be seen as multifactor; which related with genetics, lifestyle changes, less fiber consumption, increased meat and alcohol consumption, obesity, smoking, inflammatory bowel disease (IBD), and low number of routine colonoscopy screening in population at risk.[24-26]

Data regarding IBD prevalence in Indonesia mostly derived from endoscopy unit which was hospital based. IBD prevalence in Indonesia was reported 1.16-26.5%; with prevalence of ulcerative colitis (UC) between 5.4-26.5%, and Chron's Disease (CD) ranged from 1 to 10.2%.[27] Indonesia has been listed in ACCESS (Asia Pacific Chron's and Colitis Epidemiology Study) study group and was reported to have crude annual incidence (per 100,000) of 0.88 for IBD, 0.33 for CD, and 0.55 for UC. These findings were lower compared to Crude annual incidence of IBD in Asia (1.37), China (3.44), and Australia (23.67). While, Indonesia age-standarized incidence for IBD (0.83), CD (0.27), and UC (0.56) was reported.[28] Some risk factors related with increased IBD incidence are genetic predisposition, environmental factor such as smoking, increased sugar, fat, red meat intake, and low fiber diet.[29]

Gastric tumors in Indonesia is estimated to have ASR 2.8 per 100,000 population for both sexes, whereas for men by 3.9 and 1.9 for women. The findings are much lower compared to other Asian countries such as Japan (ASR 29.9), South Korea (ASR 41.8) or in the world (ASR 12,1).[22] Several studies showed the prevalence of gastric tumor ranged between 0.25 to 9.1%.[30,31] Low number of gastric tumors in Indonesia may be associated with low prevalence of H.pylori infection and the genotype which found to be less virulent.[32] Abdullah et al.[33], showed that *H. pylori* positive Japanese patients have higher gastritis incidence and grade, also higher number of atrophic gastritis and intestinal metaplasia compared with Indonesian.[33]

DEVELOPMENT OF HEALTH CARE AND GASTROENTEROLOGY EDUCATION IN INDONESIA

Indonesian Society of Gastroenterology (ISG) has cooperated with Ministry of Health Republic of Indonesia for improvement in gastrointestinal health programs. Programs that have been implemented on include the improvement and dissemination of good hygiene and sanitation, also continuation of the Ministry of Health of Indonesia programs in community health centers and hospitals as well as increased knowledge of digestive health in the community.

ISG also responsible for improvement of gastroenterology services at public hospitals and teaching hospitals or universities in Indonesia through optimal screening, diagnosis, treatment, prevention and education for patients and in cooperation with private health insurance or the National Health Insurance (*Jaminan Kesehatan Nasional*).

Research funding in the gastroenterology field has been provided by ISG through higher education directorate in the Ministry of Education and Culture Republic of Indonesia. The funding is in the form of competitive grants among Indonesia universities and also internationally. ISG also published research journal called Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy that has been established since 1995 and publishing three times a year. Every three years, National Congress (KONAS) was being held in cooperation between ISG, Indonesian Society of Digestive Endoscopy (ISDE), Indonesian Association for the Study of the Liver (Ina-ASL), and also every year there was Working National Conference (KONKER) held in 17 branches in Indonesia. Each year, ISG hold Indonesian Digestive Disease Week (IDDW) and the International Gastrointestinal Endoscopy Workshop in Jakarta, which is supported by the World Gastroenterology Organization (WGO), the Asian Pacific Association of Gastroenterology (APAGE), the American College of Gastroenterology (ACG). ISDE arranged Jakarta International Gastrointestinal Endoscopy Symposium & Live Demonstration every year since 2015. ISG initiated the establishment of educational centers for subspecialty (consultants) in gastroentero-hepatology. Currently there are 6 gastroenterology subspecialty education centers in Indonesia which located in Jakarta, Medan, Bandung, Surabaya, Yogyakarta and Semarang.[34] And also seven partial education centers located in Palembang, Bali, Makassar, Solo, Padang, Manado, and Malang. Gastrointestinal endoscopy training for internal medicine specialist, surgeon, and pediatrician has been developed in 10 educational centers.

GASTROENTEROLOGY DIAGNOSTIC MODALITY DEVELOPMENTS IN INDONESIA

Gastroenterology diagnostic modalities in Indonesia have made significant progress in detecting cancer, IBD or other functional disorders of entero-colon. Diagnosis has been using some scoring system or criteria such as Rome IV and GERD-Q that had been validated in Indonesian and combined with non-invasive or invasive examination.[35] Non-invasive examination such as gastrin and pepsinogen in serum to detect gastric cancer, detection for carcinoid using chromogranin A in serum and M2 Pyruvate Kinase (M2PK) stool test, PET CT-scan for gastrointestinal cancer staging, detection of inflammatory intestine intestinal inflammation by faecal calprotectin, elastase stool test to detect pancreatic insufficiency, *H. pylori* screening using *H. pylori* stool antigen test and urea breath test have been routinely done. Other tests using flexible or semi-flexible endoscopes, capsule endoscopy, Magnetic Resonance Cholangiopancreatography (MRCP) and endoscopy ultrasonography also been done to aid the diagnosis of gastrointestinal cancer. Endoscopic equipment in Indonesia is also supported with Narrow Band Imaging (NBI) and virtual chromoendoscopy system. There are 313 hospitals that provide services for gastrointestinal endoscopy in Indonesia based on data in 2013.[34]

GASTROENTEROLOGY THERAPEUTIC MODALITIES DEVELOPMENTS IN INDONESIA

Progress in gastroenterology therapy can be seen through the availability of medicines in

Table 7. Routinely done therapeutic endoscopy procedures in Indonesia[34]

Endoscopic procedure	Description
Upper Gastrointestinal Endoscopy	Sclerotherapy and esophageal varices ligation
	Histoacryl injection in gastric varices
	Polypectomy
	Esophagus/pyloric dilatation
	Percutaneous endoscopic gastrostomy
	Foreign body extraction
	Endoscopic Hemostasis endoscopic (clip, adrenalin injection, coagulation)
	Esophageal stenting
Lower gastrointestinal endoscopy	Polypectomy
	Endoscopic hemostasis
	Colonic stenting
Endoscopic Retrograde Cholangio-pancreatography (ERCP)	Biliary stone extraction
	Foreign body extraction
	Biliary dilatation
Enteroscopy	Enteroscopic Hemostasis
	Foreign body extraction
Endoscopic ultrasonography	Pancreatic cyst/ pseudocyst drainage
	Biliary drainage

accordance with the latest research developments and evidence-based that has been recommended by gastroenterology association around the world. Biological agents such as infliximab and adalimumab have been given to IBD-indicated patients. ISG also routinely issues several guidelines for gastroenterology diseases management in Indonesia. Therapeutic endoscopy procedure has reached significant development in Indonesia (**Table 7**).[34] Techniques that are often used for rupture esophageal varices management in Indonesia are endoscopic variceal ligation (EVL) and endoscopic injection sclerosis (EIS). Endoscopic clipping is used for other cause of gastrointestinal bleeding. Surgery for gastrointestinal polyps and cancers can also be performed with endoscopic submucosal dissection (ESD), endoscopic mucosal resection (EMR), and hot biopsy. Other type of surgery that can also be performed is laparoscopic resection. As part of integrated gastrointestinal cancer management, there are some radiotherapy centers in Indonesia which already well-established such as in Dharmais National Cancer Hospital, Cipto Mangunkusumo Hospital, Hasan Sadikin Hospital, Gading Pluit Hospital, and etc.

CONCLUSION

Indonesia as developing country is facing high burden of gastrointestinal tropical and infectious diseases, however, during the last few years there were also increased number of non-infectious gastrointestinal diseases such as GERD, IBD, gastric and colorectal cancer.

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