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INCIDENCE AND CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE IN BRUNEI DARUSSALAM.

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ABSTRACT

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Keywords: Inflammatory bowel disease, Incidence, Crohn's disease, Ulcerative colitis

INTRODUCTION

The global incidence of inflammatory bowel disease (IBD) which consist mainly of Ulcerative Colitis (UC) and Crohns Disease (CD) is increasing and its emergence in Asian countries has been attributed to the modernisation with change in diet and lifestyle.[1] In developed nations, such as Europe and North America, the reported annual incidence rates of IBD have been between 20.2 and 24.3 per 100,000 population.[2] While it is less common in Asia, there have been reports of increasing incidence rates. East Asian countries, such as South Korea, Japan and China have reported incidence rates ranging between 0.54 and

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3.44 per 100,000 population. Singapore and Malaysia, two neighbouring nations to Brunei Darussalam have reported lower incidence rates of 1.06 and 0.94 per 100,000 population, respectively.[3] These reflect that IBD are still uncommon in the Southeast Asian region compared to developed nations.

It is well established across Western countries that IBD is more prevalent in Caucasian and Ashkenazi Jewish.[4] In Asia where there are multi-ethnic populations, certain ethnic groups are more affected. In Southeast nations such as Singapore and Malaysia with multi ethnic populations, Indians have higher incidence.[1] Western and Asian studies have contradicting results when comparing between genders. Western studies found an overall predominance of IBD in females while Asian studies reported predominance in males.[4] Western studies reported that females had 20-30% higher risk of suffering from CD [5] but Asian studies stated males were at a higher risk.[4] However, both Western and Asian studies have not found a gender predominance in the occurrence of UC.[5] As for the mean age at diagnosis, Western studies reported a peak age of onset at 20-30 years for CD and 30-40 years for UC.[3] Patients in Asia were found to be slightly older, with peak age of diagnosis at around 20-39 years for CD and 35-44 for UC.[6]

Clinical studies reported that 95% of UC patients mainly present with bloody stools, and some complain of tenesmus and abdominal pain.[7] CD can present similarly to UC but its main presenting complaints are chronic diarrhoea, abdominal pain and weight loss. UC and CD patients can also present with fever, but it is noted to occur more frequently in CD patients.[8] Terminal ileum and the proximal colon are the most affected segments of the gastrointestinal tract in CD patients. UC is usually confined to the rectosigmoid area and in 20-30% of UC patients the disease extends beyond the hepatic flexure.[5]

At present, there is no published data on IBD in Brunei Darussalam. Due to increasing global incidence rates of IBD, it is important to publish baseline incidence rates of IBD and its presenting characteristics within the Bruneian population for future trend comparison. Thus the aim of this study is to assess the incidence and characteristics of IBD in Brunei Darussalam, a developing Southeast Asian nation with a predominant Malay population.

MATERIALS AND METHODS

The study is a retrospective cross-sectional chart review of patients with confirmed histological diagnosis of IBD, identified from the Disease Registry maintained by the Department of Pathology, Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital. Ethic approval was obtained from the Medical Health Research Ethic Committee, Ministry of Health.

Patient Population

Patients diagnosed with UC and CD between 2000 and 2017 were identified through the pathology registry maintained by the Department of Pathology, RIPAS Hospital. Information available from this registry include demographic detail and date of diagnosis. Diagnoses of IBD were based on established criteria of clinical presentations, endoscopic changes, laboratory and characteristic histological features. The histological features used to differentiate between UC and CD were in accordance with the 9th edition of Rosai and Akerman's Surgical Pathology.[9] Histopathological features of UC included crypt architectural distortion, mononuclear cell infiltration of the lamina propria, mucin depletion and diffuse basal plasmacytosis. While for CD granulomatous inflammation, polynuclear leucocyte infiltration of the lamina propria and presence of epithelioid granuloma and basal giant cells were observed.[9] Patients who attended consultations at Jerudong Park Medical Centre (JPMC) were excluded as details of their

presentation and management could not be accessed.

Data Collection

Once the patients were identified, the Brunei Health Information Management system (Bru-HIMS) database which was started in 2013 was used to access clinical notes. Clinical data at the time of diagnosis such as age, race, gender, presenting symptoms and extend of disease were collected from the database. For patients diagnosed before implementation of Bru-HIMs, prospectively collected data on patient diagnosed with IBD held by the Division of Gastroenterology and Hepatology was also retrospectively reviewed. This database contains all demographic and clinical information (type of IBD, date of diagnosis, age of diagnosis, clinical presentations and disease extend and severity).

The data was collected using performa that was designed for this study and transposed to Microsoft Excel for analysis.

Statistical analysis

Statistical analysis was done through Statistical Package for Social Sciences (SPSS), version 23.0. The population census used to calculate the incidences were retrieved from the public website of the Ministry of Health, Brunei Darussalam.[10] Where possible, categorical variables were analysed using Pearson's Chi-Square. However, when the assumptions for Pearson's Chi-Square were not met, Fisher's exact test was used instead. *P* values less than 0.05 ($p<0.05$) were considered as significant and all *p* values were corrected to 2 decimal places.

RESULTS

The incidence of IBD was found to be generally increasing between 2004 and 2016, rising from 0.28 per 100,000 to 3.08 per 100,000 population (Figure 1). Rising trends were also seen in UC (Figure 2) and CD (Figure 3). The increase was more pronounced for UC compared to CD.

Overall, IBD was more common among males, 49 (59.0%), compared to females, 34 (41.0%). Ethnic breakdown of the patients diagnosed with IBD was consistent

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total number of IBD	1	4	1	5	3	3	5	1	3	6	1	3	8
Incidence per 100,000 population	0.28	1.08	0.26	1.28	0.80	0.79	1.29	0.25	0.75	1.48	0.24	0.72	3.08

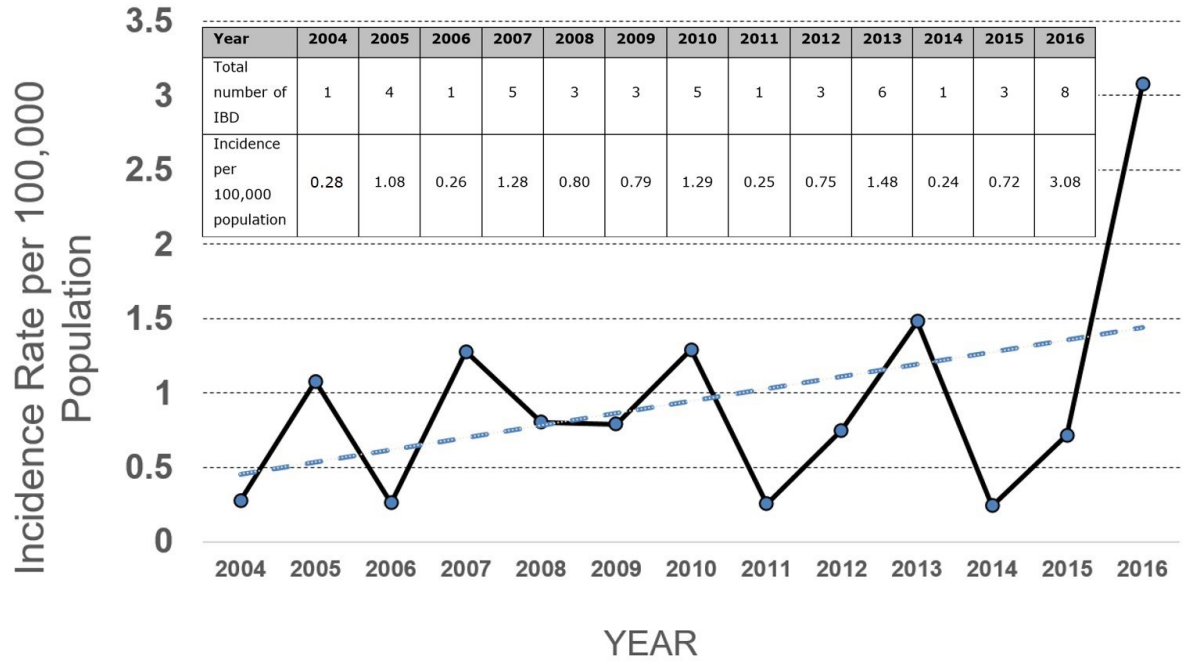

Figure 1: Line graph of Incidence of Inflammatory Bowel Disease (2004 – 2016) with trend line by year.

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total number of UC	1	2	0	3	3	1	4	1	1	6	0	3	5
Incidence per 100,000 population	0.28	0.54	0	0.77	0.80	0.26	1.03	0.25	0.25	1.48	0	0.72	1.66

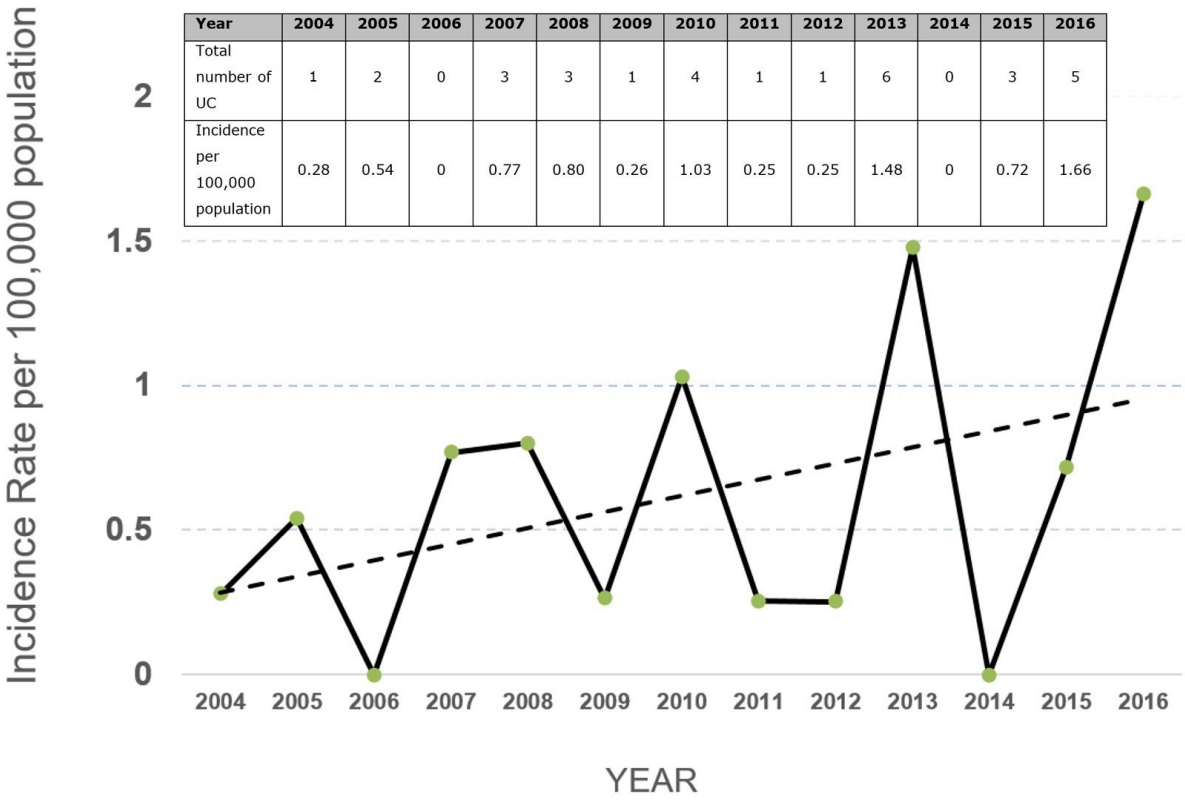

Figure 2: Line graph of Incidence of Ulcerative Colitis (2004 – 2016) with trend line by year.

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total number of CD	0	2	1	2	0	2	1	0	2	0	1	0	3
Incidence per 100,000 population	0	0.54	0.26	0.51	0	0.53	0.26	0	0.50	0	0.24	0	1.42

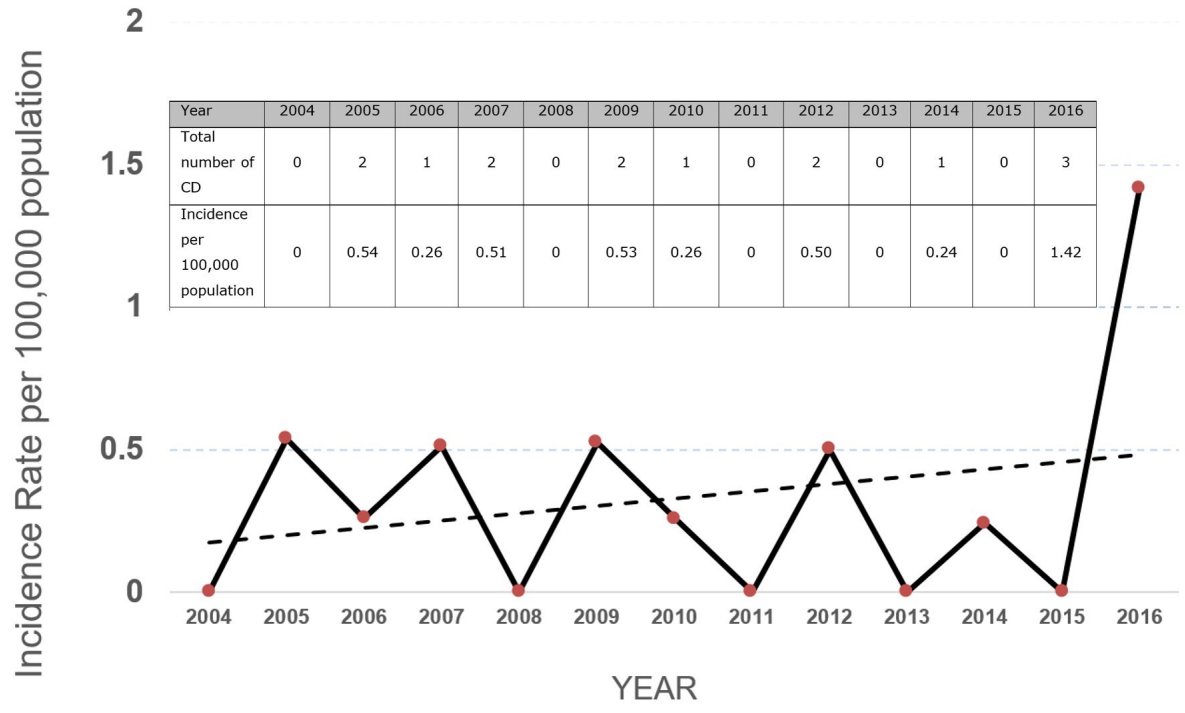

Figure 3: Line graph of Incidence of Crohns Disease (2004 – 2016) with trend line by year.

Figure 3: Line graph of Incidence of Crohn's Disease (2004 – 2016) with trend line by year.

Variable	Mean (SD)	*n* (%)
Age (year)	36.0 (17.2)	
Gender (n=83)		
Malay		50 (60.2)
Chinese		16 (19.3)
Others		17 (20.5)
Diagnosis (n=83)		
CD		27 (32.5)
UC		56 (67.5)
Family History of IBD (n=83)		2 (2.4)

SD : Standard Deviation; CD : Crohns disease; UC : Ulcerative colitis

with the national breakdown. The mean age of diagnosis for IBD was 36.0 ± 17.2, (range: 3 to 83 years) There were more cases of UC seen (67.5%) than CD (32.5%). UC was twice more common than CD (Table 1).

Comparisons between CD and UC showed significant differences in mean age at diagnosis and presenting complaints. The mean age at diagnosis of CD (32.1 ± 13.6) was younger than UC (40.5 ± 17.5), (p=0.010). CD patients were less likely to complain of bleeding per rectum/bloody diarrhoea (p<0.001) and diarrhoea (p=0.003) compared to UC patients. Details are summarised in Tables 1 and 2.

DISCUSSION

In Asia, the incidence of IBD is increasing but the incidence rates remain lower than in European countries and North America.[3] Our study found that in Brunei Darussalam, there is also an increasing incidence of IBD with the annual rate ranging from 0.28 to 3.08 per 100,000 population between 2004 and 2016. While the annual incidence rates are lower than our European counterparts, our highest incidence rate has surpassed annual rates of some of our neighbouring countries, such as Singapore (1.06 per 100,000 population) and Malaysia (0.94 per 100,000 population).[3]

The trends showed both UC and CD to be increasing, more for UC than CD. The UC trend showed a sharper increase in the number of cases and generally higher number of annual incidence rates when compared to the CD trend. There were wide fluctuations in the trends and this was due to the overall small number of cases, reflecting the size of the population. However, the total number of cases can be considered an accurate representation of the whole country as it included all histology proven cases that presented to healthcare services. In Brunei Darussalam, there is only one central pathology department that processes all tissue samples, hence capturing all histology proven cases.

In previous studies, the incidence of IBD was found to differ significantly between different ethnic groups and genders. In our study, the ethnic groups were broken down into Malay (60.2%), Chinese (19.3%) and others (20.5%). This ratio of roughly 3:1:1 generally resembled the ethnic breakdown of the population of Brunei Darussalam suggesting IBD affects each ethnic group equally. On the other hand, Malaysia, a country with almost similar population ethnicity breakdown, demonstrates a higher incidence rate in Indians, followed by the Chinese and the Malays.[3] Our study population included a small number of Caucasian and Indian expatriate populations. Most of the Indian population works in the industrial sector and hence, when diagnosed with chronic diseases requiring long-term treatment, tend to return to their homeland.

When comparing the incidence of CD and UC between males and females, Western studies have reported that females had higher risk of developing CD[5] while Asian studies have reported males had higher risk.[4] In both Western and Asian studies, there were no gender predominance found in UC patients.[5]

Table 2: Comparison of demographic data and characteristics between CD and UC.

Variable	CD *n* (%)	UC *n* (%)	x^2 statistics (df)	*p* value
Mean age (year)	28.4 ± 13.9	39.6 ± 17.6		0.005[a]
Gender (CD=27;UC=56)				
Male	19 (70.4)	30 (53.6)	2.13 (1)	0.145[b]
Female	8 (29.6)	26 (46.4)		
Ethnicity (CD=27;UC=56)				
Malay	15 (55.6)	35 (62.5)	2.19 (1)	0.334[b]
Chinese	4 (14.8)	12 (21.4)		
Others	8 (29.6)	9 (16.1)		
Presenting Complaints (CD=27;UC=52)				
BPR/Bloody Diarrhoea	4 (14.8)	40 (76.9)	27.78 (1)	0.000[b]
Diarrhoea	11 (40.7)	38 (73.1)	7.89 (1)	0.005[b]
Abdominal Pain	13 (48.1)	28 (53.8)	0.23 (1)	0.631[b]
Fatigue	1 (3.7)	7 (13.5)		0.253[c]
Fever	2 (7.4)	9 (17.3)		0.315[c]
Weight Loss	9 (33.3)	4 (7.7)		0.008[c]
Loss of Appetite	2 (7.4)	12 (23.1)		0.122[c]
Tenesmus	2 (7.4)	16 (30.8)	5.51 (1)	0.019[b]

df : degree of freedom; CD : Crohns disease; UC : Ulcerative colitis; [a]Independent *t* test; [b]Pearson's Chi-square test; [c]Fisher's exact test

Our data supports Asian studies, whereby males are more likely to be affected by CD but there seems to be no gender predilection for UC. While the overall incidence is higher in males than females, when comparing the proportions of males and females suffering from CD or UC, it was found that males and females have an equal risk of developing either disease (p=0.145). However, this result may be due to the overall small number of patients affected. Longer term study with more patient studied may provide better understanding.

The mean age at diagnosis for IBD was found to be 36.0 ± 17.2 years old. Additionally, it was found that the age at diagnosis for CD (28.4 ± 13.6 years) is significantly lower than the age of diagnosis for UC (39.6 ± 17.6 years), (p=0.005). This is similar to numerous studies which report the age of CD occurrence is younger than the age of UC occurrence.[3] However, both means are slightly higher than the reported range in in the United Kingdom, where the median age of diagnosis for CD and UC is 30 and 39 years old respectively.[11] On the other hand, Asian studies report a younger median age at diagnosis. In Japan, the median age at diagnosis was reported to be 22 years old for CD[12] while in China, it was reported to be 25 years for UC.[13] Perhaps, the late presentation in age in this country could partly be due to exclusion of a differential diagnosis of IBD by clinicians or patients' not recognising the significance of their symptoms. A small proportion of mild disease may escape detection if patients have mild forms of the disease and do not proceed to undergo colonoscopy whereas most moderate to severe cases will eventually be diagnosed by colonoscopy and biopsy.

The symptoms recorded in this study

were typical signs of chronic gastrointestinal tract inflammation. Depending on the affected sites, chronic inflammation can lead to ulcerations and loss of mucosal function, resulting in pain, presence of blood in stools and malabsorption of nutrients. Out of the 27 CD patients, 14.8% experienced rectal bleeding or bloody diarrhoea while 76.9% of 52 UC patients experienced it. Similarly, 40.7% of CD and 73.1% of UC patients experience diarrhoea and 7.4% of CD and 30.8% of UC presents with tenesmus. Thus, is a significantly larger proportion of UC patients experiencing rectal bleeding/bloody diarrhoea (p<0.001), diarrhoea (p=0.005) and tenesmus (p=0.019), which is consistent with most literature.[7, 14] CD patients reported a higher likelihood of experiencing weight loss compared to UC patients (p=0.008). Other common symptoms such as abdominal pain (p=0.631), fatigue (p=0.253), fever (p=0.315) and loss of appetite (p=0.122) were present in both CD and UC patients but there was no significant difference in the proportions between the two groups.

Most studies show that approximately 30-50% of UC patients are affected in rectosigmoid area while in CD, the terminal ileum is the area most affected. [5] The findings of this study was similar – out of 19 CD patients, 36.8% were affected at the terminal ileum, 52.6% at the caecum, 36.8% at the rectum while out of 49 UC patients, the corresponding percentages of areas affected were 14.3%, 26.5% and 87.8% respectively. This finding can be related to common UC complaints identified in this study. As the rectum is more likely to be involved, rectal manifestations, such as rectal bleeding and tenesmus, would be more common in UC patients rather than CD patients. Unlike most studies, however, our study detected 12.2% of 49 UC patients with rectal sparing, greatly contrasting the reported 0% of absolute rectal sparing in an American study. Initially, the study suggested the experience of 31% prevalence rate of relative rectal sparing but upon histological analysis, most of the 31% had architectural distortion in the rectal mucosa.[9] Similarly, in our 11.9% of UC patients, there may be slight rectal involvement, which perhaps was not biopsied to be confirmed histologically. Hence, the actual percentage of UC patients with absolute rectal sparing cannot be concluded. Moreover, upper gastrointestinal involvements appear to be uncommon for CD patients based on symptoms are presentation. However, this observation may be inaccurate as systematic evaluations, such as upper GI endoscopy or imaging, are not routinely carried out in the absence of symptoms in our setting. Therefore, data regarding the oesophagus, stomach and small intestine cannot be provided. To date, there has been one CD patient with nodular mucosal manifestations in the stomach which resolved with treatment.

It is note-worthy that various studies have been made regarding family history and the occurrence of IBD. Overall, positive family history for IBD is reported in 5–16% of CD patients and 8–14% of UC patients.[15] Mutations at disease-predisposing loci on chromosome 16q, which can be inherited, can result in loss of intestinal mucosal function, leading to a higher risk of developing IBD.[16] Our study only identified two UC patients with a positive family history, neither of whom represented the local population. An explanation could be that IBD is still at its early stages of emergence in Brunei Darussalam, and so a pattern of family history of IBD would not yet be established nor recognised within the population.

CONCLUSION

This study shows that the incidence of IBD is increasing in Brunei Darussalam. Patients with UC were older than CD patient at diagnosis consistent with what have been reported in the literature. However, we did not find any gender and ethnic propensity. The significance

and novelty of this study is that being the only available data on the incidence and characteristics of IBD in Brunei Darussalam, it can serve as a baseline reference for future studies on IBD.

DISCLOSURE

All authors have contributed to the manuscript equally. None of the authors have direct or financial conflicts of interest with this paper and material contained herein.

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