MEDICAL SCIENCE

Assessment of Saudi medical students' knowledge about microbiota, dysbiosis and gut-brain interplay in neuropsychiatric disorders

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ABSTRACT

Background: Gut microbiome is a vast microorganism's ecosystem that resides in the human gastrointestinal tract. Microbiota can have a complex crosstalk with the central nervous system, creating "gut–brain axis", playing a crucial role in neuropsychiatric disorders pathogenesis. *Aim:* This study aimed to assess knowledge about human gut microbiota, dysbiosis and gut-brain interplay in neuropsychiatric disorders among Saudi medical students. *Methods:* This is a descriptive cross-sectional study using questionnaires to collect the data, targeting senior medical students and interns in Saudi Arabia from November 2022 to January 2023. *Results:* Overall, our study shows that our students possess adequate general knowledge about microbiota, dysbiosis and probiotics; however, they lack sufficient knowledge regarding gut-brain axis and dysbiosis role in the context of neuropsychiatric diseases pathogenesis and management. *Conclusion:* Developing the medical curricula and adopting more modalities of learning strategies to discuss the most recent scientific advances in different medical topics are crucial to enhance medical students' knowledge acquisition, thus providing adequate recommendation to their future patients and community.

Keywords: Microbiota, Dysbiosis, Gut-Brain axis, Saudi Arabia

1. INTRODUCTION

The gut microbiota comprises a complex ecosystem of commensal microorganisms inhabiting the human gastrointestinal tract. The gut microbiota is composed of four main phyla (*Bacteroidetes*, *Proteobacteria*, *Firmicutes* and *Actinobacteria*) and two other phyla (Fusobacteria and Verrucomicrobia), interacting with each other and the host intestinal epithelium, maintaining the mucosal barrier integrity and acting as immunomodulators to prevent infections (Stopińska et al., 2021). These effects referred to released short-chain fatty acids like butyrate and acetate, which

have anti-inflammatory and anti-proliferative roles against malignant cells (Aljahdali, 2022).

The innate and adaptive immunity responses have recently been reported to be influenced by gut microbiota, both locally and systemically, impacting distant systems (Ochoa-Repáraz et al., 2017). Many factors, even before birth, shape the developing microbiota, including genetics, stress, diet, medication and environmental factors (Cowan et al., 2020). According to WHO, probiotics are 'live microorganisms which when administered in sufficient amounts confer a health benefit on the host', they can be found in food, drinks and medication, containing different beneficial bacteria including *Lactobacillus* and *Bifidobacterium* that can colonize the gut and provide a healthier balance of microflora (Barqawi et al., 2021).

Microbiota–gut–brain axis refers to the bidirectional communication between the gut microbiota and the brain. The autonomic nervous system, the vagus nerve, the enteric nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, the neuroendocrine system and the immunological pathway are among the many communication pathways that make up this axis (Ojeda et al., 2021). Also, as a part of this microbiota–gut–brain axis, it has been recognized that the microbiota is a modulator of brain and behavior (Cowan et al., 2020).

The strict balance between pathogenic microbes and alternative probiotic populations is crucial in modulating systemic inflammation and neuronal health. Gut-microbiota alterations have been attributed to different neuropsychiatric and neurodegenerative conditions. Moreover, proper dieting improved neurodegenerative disorders by restoring the balance between pathogenic microbes and probiotic populations (Włodarek, 2019; Zhu et al., 2020). Neurodegenerative diseases are still public health issues diminishing life quality, posing significant financial and social burdens.

Neurodegenerative illnesses have been found to be widespread in the Arab world, affecting between 1.1-2.3% of people under the age of 50 and 13.5-18.5% of people over the age of 80. It has been established that a variety of factors, including age, education, gender, genetics and medical conditions influence the prevalence of neurodegenerative illnesses. Notably, type-2 diabetes and hypertension have been shown to promote the onset of neurodegenerative disorders through neuroinflammation, which accounts for part of the high prevalence in Arab countries (El-Metwally et al., 2019). Therefore, further studies aiming to relieve and control these disorders are critical to improve these patients' lives quality.

Alzheimer's disease is a prevalent neurodegenerative disorder, where the prevalence in Saudi Arabia is 5.2-3.85% (El-Metwally et al., 2019). The etiology of Alzheimer's disease has not been completely illustrated, but emerging data indicates that there is a link between gut microbiota with Alzheimer's disease. Microbiome alterations were reported in human fecal samples, including decreased anti-inflammatory, but increased pro-inflammatory bacteria in Alzheimer's disease patients in comparison with healthy controls, with a positive correlation of increased pro-inflammatory cytokines blood levels and abundance of *Escherichia/Shigella* (Cattaneo et al., 2017; Vogt et al., 2017).

Parkinson's disease, the second most prevalent neurodegenerative disease, is characterized by α-synuclein protein aggregation in the substantia nigra pars compacta of the midbrain, as the main hallmark (Man et al., 2021). Notably, it has been reported that there is a significant alteration in the abundance of certain microbiota families in Parkinson's disease patients affecting different populations in comparison to control, correlated with disease manifestation. Authors suggested that these dysbiosis might lead to the impaired short-chain fatty acids production, lipid metabolism, intestinal permeability and immunoregulatory function contributing to disease pathogenesis (Shen et al., 2021).

Another common neurodegenerative disorder, multiple sclerosis, affecting approximately 40.4/100,000 in the general population of Saudi Arabia and 61.95/100,000 in Saudi nationals. It mostly affects young adults particularly women, so it is called "the great crippler of young adults" (Al-Jumah et al., 2020). The clinical picture differs from one patient to another; mostly including physical, cognitive, psychological and emotional symptom, impacting the productivity and quality of life of these patients (GBD 2016 Multiple Sclerosis Collaborators, 2019).

Ample studies have revealed that patients with multiple sclerosis show microbial dysbiosis, i.e., a reduction in beneficial bacteria and rise in harmful bacteria (Freedman et al., 2018). Furthermore, relapsing-remitting multiple sclerosis patients have shown an altered microbiota composition in comparison with healthy people. So, the restoration of the normal count of these populations could reduce the immune system reactivation and inflammatory reactions (Schepici et al., 2019).

According to Global Burden of Disease Study 2015, depressive disorders and anxiety disorders are the fourth and sixth leading causes of disability in KSA (Altwaijri et al., 2020). It has been reported that gut microbiota in anxiety and depressive disorders is characterized by a relative reduction of bacteria that produce short-chain fatty acids and a relative increase of pro-inflammatory species (Simpson et al., 2021). A meta-analysis reported depression scores decline in major depressive disorder patients after restoration of the microbiota with probiotics supporting the interplay between the gut microbiota and depression (Huang et al., 2016).

The medical students and interns are the healthcare professionals of the future, so, they should have more knowledge about microbiota, probiotics and impact on neuropsychiatric disorders to give the appropriate recommendation to their community and patients. Thus, we went through this work to assess medical students' knowledge about human microbiota, dysbiosis, probiotics, as well as role of dysbiosis in gut brain axis and different neuropsychiatric disorders.

2. MATERIALS AND METHODS

Study design and sampling

This is a descriptive cross-sectional study, where self-structured questionnaire was used to target senior medical students and interns at Saudi Medical Colleges, from November 2022 to January 2023. The sample size was calculated according to Cochran equation (Cochran, 1977) of simple random sampling, as given below.

$$n = z^2 [P (1 - P)/(D^2)],$$

n is the sample size, z is the standard variable of the normal distribution corresponding to 95% confidence level, P is the anticipated population proportion of knowledge about microbiota and gut-brain axis, d is the absolute statistical precision on either side of the anticipated population proportion. We proposed the probability of having good knowledge of microbiota and gut-brain axis is 50% and d = 0.05; then, the initial sample size was= $1.962 * 0.5 * 0.5/0.0025 = 385$

Questionnaire design and data collection

The authors developed a self-structured questionnaire based on reviewing the international current literature. Data was collected online through Google Forms posted on the Internet platforms and on social media platforms. Data was stored on a network-attached storage solution, the cloud.

The informed consent form, questionnaire description, the aim of study and data confidentiality was provided on the first page of the questionnaire. The questionnaire is composed of 3 sections (28 questions). The first section includes general information about the participant; second section focuses on the participants' knowledge about the microbiota, dysbiosis and probiotics. Third section assesses the participants' knowledge regarding gut-brain interplay in neuropsychiatric disorders among Saudi medical students.

To assess knowledge, a point was given for either confirming a correct statement or disagreeing with an incorrect one and the total score was calculated. Then, a total score ≥70% was considered as acceptable, 50% to <70% as moderate and < 50% as low level of knowledge. All clinical years medical students (4^{th}, 5^{th} and 6^{th}), in addition to medical interns in Saudi Arabia Universities are eligible to be included in the study. Students who didn't fill in the questionnaire properly were excluded from the study.

Statistical Analysis

The data were organized and tabulated using IBM's SPSS version 20 (Statistical Package for Social Studies), which was developed in Chicago, Illinois. Numbers and percentages for each variable were calculated using descriptive statistical techniques. The statistical correlations between participant characteristics and knowledge scores were evaluated using the chi-squared test. $P< 0.05$ is the statistical threshold for significance.

3. RESULTS

Characteristics of participants

The total number of participants is 379. Table 1 shows characteristics of participants. Females represent 64.1%. About one quarter of students (28.2%) is from the middle region, 23.7% are from northern regions, whereas only 20.3% are from eastern regions, 14.2% from southern regions and 13.5% are from western regions. Most of participants (54.1%) are 4^{th} year medical students. About half of participants (51.2%) have 3.5-4 GPA.

Assessment of knowledge about the microbiota, dysbiosis and probiotics

The overall correct answer rate of the knowledge questions is 65.6% and the ranges of correct answer rates for all students are 47.2% to 90.0%. Among participants, 69.4% know the term 'microbiota' and 61.5% understand that microbiota composition is different between different population and ethnicities. The majority of students (90.0%) understand that presence of bacteria in the gut can be beneficial to humans. Only 47.2% give a correct answer when asked if there is an interaction between gut microbiota and brain. Also, the definition of dysbiosis is reported among 56.7% of students. More than half of students know that probiotics products could be effective in inflammatory diseases (Table 2).

Table 1 Characteristics of participants

Variables		N (%)
Gender	Female	243 (64.1%)
	Male	136 (35.9%)
Region	Eastern	77 (20.3%)
	Middle	107 (28.2%)
	Northern	90 (23.7%)
	Southern	54 (14.2%)
	Western	51 (13.5%)
Academic level	4th year	205 (54.1%)
	5th year	58 (15.3%)
	6th year	47 (12.4%)
	Medical interns	69 (18.2%)
GPA	3-3.5	148 (39.1%)
	3.5-4	194 (51.2%)
	Less than 3	37 (9.8%)

Table 2 Participants' knowledge about the microbiota, dysbiosis and probiotics

Variable	Correct	I don't know	Incorrect
The term 'microbiota' refers to all microorganisms in the human body	263 (69.4%)	47 (12.4%)	69 (18.2%)
There are microorganisms naturally living in the gut	333 (87.9%)	19 (5.0%)	27 (7.1%)
Microbiota composition is different between different population and ethnicities	233 (61.5%)	94 (24.8%)	52 (13.7%)
Not all microorganisms can cause an infection	199 (52.5%)	43 (11.3%)	137 (36.1%)
Presence of bacteria in the gut can be beneficial to humans	341 (90.0%)	13 (3.4%)	25 (6.6%)
There is an interaction between gut microbiota and brain	179 (47.2%)	152 (40.1%)	48 (12.7%)
Dysbiosis refers to altered microbiota in the human body	215 (56.7%)	139 (36.7%)	25 (6.6%)
Antibiotics can alter the gut microbiota composition	319 (84.2%)	38 (10.0%)	22 (5.8%)
Stress can alter the gut microbiota composition	278 (73.4%)	71 (18.7%)	30 (7.9%)
Alteration of gut microbiota may be associated with inflammatory diseases	291 (76.8%)	68 (17.9%)	20 (5.3%)
Alteration of gut microbiota may be associated with metabolic disorders such as obesity	227 (59.9%)	110 (29.0%)	42 (11.1%)
Probiotics can be consumed as supplements or probiotics-fortified foods to remodel the microbiota composition	225 (59.4%)	120 (31.6%)	34 (9.0%)
Probiotics could increase the secretion of anti-inflammatory cytokines	191 (50.4%)	163 (43.0%)	25 (6.6%)
Probiotics products could modulate immune responses	206 (54.4%)	149 (39.3%)	24 (6.3%)
Probiotics products could be effective in inflammatory diseases	230 (60.7%)	131 (34.6%)	18 (4.7%)

Assessment of Knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases

The overall correct answer rate of the knowledge questions is 54.68%, and the ranges of correct answer rates for all students are 40.7% to 67.8%. About two thirds of participants know the pathogenesis of neurodegenerative diseases. Only 27.7% of participants have a family history of any neurodegenerative diseases. About half of the undergraduates know examples of probiotic products and know that probiotics intake can improve one's mood and state of mind. Only 47.5% know that modification of gut microbiota may be an additional therapeutic strategy for anxiety and depressive disorders. 67.3% of students report that fecal microorganisms can be transplanted from a healthy to a sick individual to remodel gut microbiota as a therapeutic strategy (Table 3).

Table 3 Participants' Knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases

Variable	Yes	No
Do you know the pathogenesis of neurodegenerative diseases?	257 (67.8%)	122 (32.2%)
Do you have a family history of any of neurodegenerative diseases?	105 (27.7%)	274 (72.3%)
Do you know examples of probiotic products?	190 (50.1%)	189 (49.9%)
Do you know that there are differences in the gut microbiota composition of neurodegenerative diseases patients compared to healthy controls?	202 (53.3%)	177 (46.7%)
Do you know that modification of gut microbiota may be an additional therapeutic strategy for neurodegenerative diseases?	154 (40.7%)	225 (59.4%)
Do you know that probiotics intake can improve one's mood and state of mind?	209 (55.1%)	170 (44.9%)
Do you know that there are differences in the gut microbiota composition of anxiety and depressive disorders patients compared to healthy controls?	211 (55.7%)	168 (44.3%)
Do you know that modification of gut microbiota may serve as an additional therapeutic strategy for anxiety and depressive disorders?	180 (47.5%)	199 (52.5%)
Do you know that fecal microorganisms can be transplanted from a healthy to a sick individual to remodel the gut microbiota as a therapeutic strategy?	255 (67.3%)	124 (32.7%)

The average knowledge score about microbiota, dysbiosis and probiotics among the students is 9.3±3.1. Undergraduates who have scores above 10 are 35.9% (n=136) indicating an acceptable level of knowledge and only 26.1% have low level of knowledge. Regarding the Knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases, the average score is 4.3±2.5. Undergraduates who have scores 6 and more are 36.4% indicating an acceptable level of knowledge, whereas 42.2% of students have a low level of knowledge (Table 4) (Figure 1).

Table 4 Total knowledge scores among participants

Participants' knowledge about the microbiota, dysbiosis and probiotics	Acceptable	136 (35.9%)
	Moderate	144 (38.0%)
	Low	99 (26.1%)
	Total scores	9.3±3.1
Participants' Knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases	Acceptable	138 (36.4%)
	Moderate	81 (21.4%)
	Low	160 (42.2%)
	Total scores	4.3±2.5

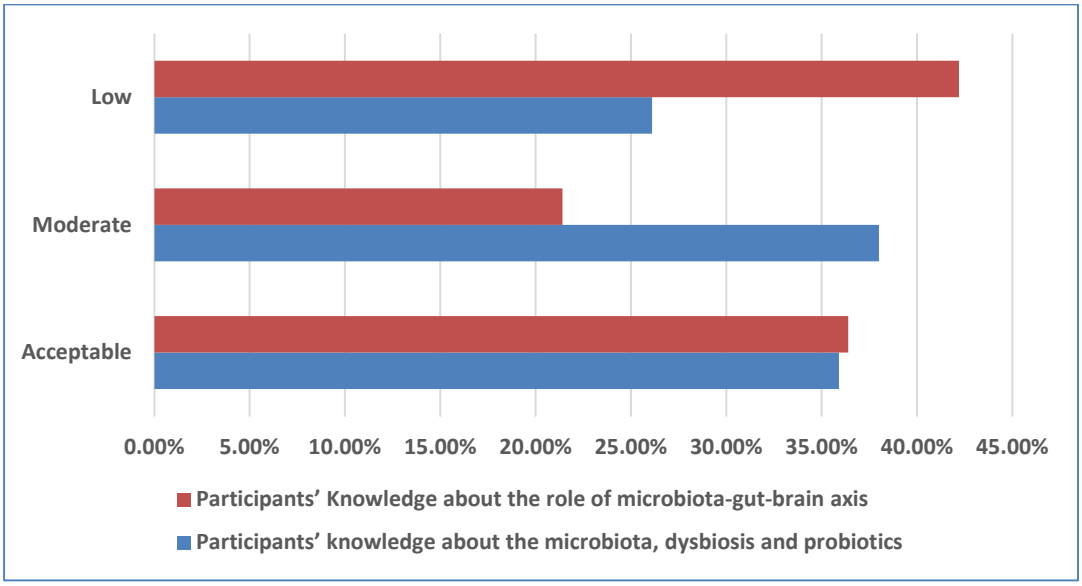

Figure 1 Total knowledge scores among participants

Table 5 and Figure 2, 3, 4 and 5 indicate the relation between participants' knowledge and their characteristics. 59.6% of females have an acceptable level of knowledge about the microbiota, dysbiosis and probiotics in comparison with 40.4% of male students. 32.4% of students from the middle region have an acceptable level of knowledge, whereas only 9.6% of students in the western region. Of the students in the 4th grade, 38.2% have a significantly acceptable knowledge than other grades (p=0.00*). 59% of students with 3.5-4 GPA could have an acceptable knowledge in comparison with others.

In addition, females significantly have an acceptable knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases (53.6%) comparing with 46.4% of male students (p =0.004*). Students from the middle region had a significant acceptable knowledge (39.1%) in relation to other regions (p=0.00*). About half of 4th grade students (51.2%) had a significant acceptable and moderate levels of knowledge (p=0.00*). Students who have GPA 3.5-4 have a significant acceptable knowledge (59.4%) comparing with other students (p=0.00*).

Table 5 Relation between participants' total knowledge and characteristics of the studied students

A. Participants' total knowledge about the microbiota, dysbiosis and probiotics		Acceptable	Moderate	Low	p value
Gender	Female	81 (59.6%)	92 (63.9%)	70 (70.7%)	0.2
	Male	55 (40.4%)	52 (36.1%)	29 (29.3%)	
Region	Eastern	36 (26.5%)	21 (14.6%)	20 (20.2%)	0.08
	Middle	44 (32.4%)	38 (26.4%)	25 (25.3%)	
	Northern	29 (21.3%)	41 (28.5%)	20 (20.2%)	
	Southern	14 (10.3%)	24 (16.7%)	16 (16.2%)	
	Western	13 (9.6%)	20 (13.9%)	18 (18.2%)	
Academic level	4th year	52 (38.2%)	90 (62.5%)	63 (63.6%)	0.00*
	5th year	25 (18.4%)	21 (14.6%)	12 (12.1%)	
	6th year	16 (11.8%)	18 (12.5%)	13 (13.1%)	
	Medical interns	43 (31.6%)	15 (10.4%)	11 (11.1%)	
GPA	3-3.5	45 (33.1%)	57 (39.6%)	46 (46.5%)	0.06
	3.5-4	81 (59.6%)	73 (50.7%)	40 (40.4%)	
	Less than 3	10 (7.4%)	14 (9.7%)	13 (13.1%)	
B. Participants' total Knowledge about Microbiota-gut-brain axis as a key to neuropsychiatric diseases					

Gender	Female	74 (53.6%)	60 (74.1%)	109 (68.1%)	0.004*
	Male	64 (46.4%)	21 (25.9%)	51 (31.9%)	
Region	Eastern	41 (29.7%)	14 (17.3%)	22 (13.8%)	0.00*
	Middle	54 (39.1%)	18 (22.2%)	35 (21.9%)	
	Northern	23 (16.7%)	22 (27.2%)	45 (28.1%)	
	Southern	12 (8.7%)	14 (17.3%)	28 (17.5%)	
	Western	8 (5.8%)	13 (16.0%)	30 (18.8%)	
Academic level	4th year	57 (41.3%)	48 (59.3%)	100 (62.5%)	0.00*
	5th year	19 (13.8%)	11 (13.6%)	28 (17.5%)	
	6th year	15 (10.9%)	12 (14.8%)	20 (12.5%)	
	Medical interns	47 (34.1%)	10 (12.3%)	12 (7.5%)	
GPA	3-.5	41 (29.7%)	46 (56.8%)	61 (38.1%)	0.00*
	3.5-4	82 (59.4%)	24 (29.6%)	88 (55.0%)	
	Less than 3	15 (10.9%)	11 (13.6%)	11 (6.9%)	

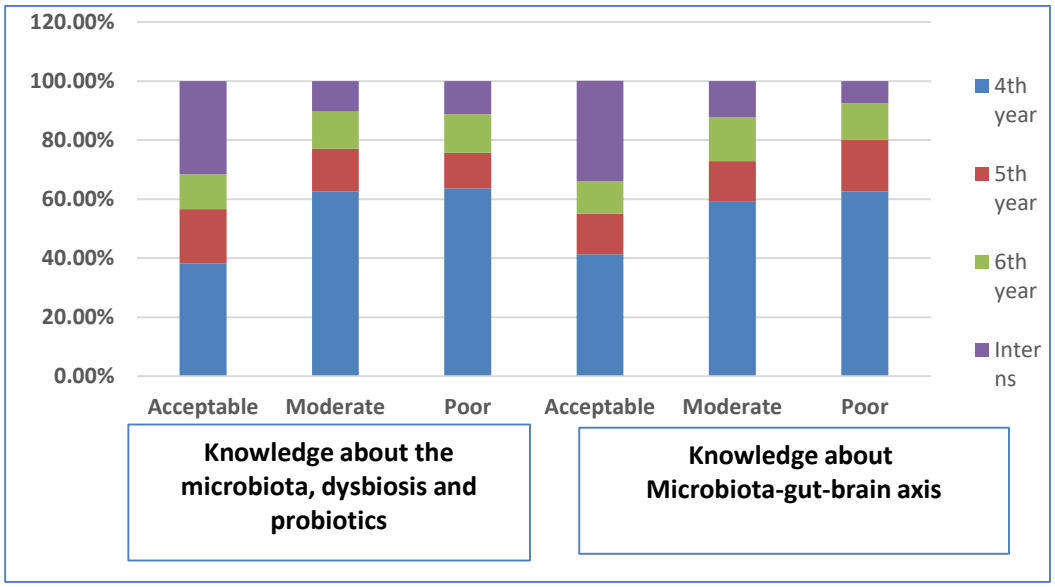

Figure 2 Relation between participants' total knowledge and their academic level

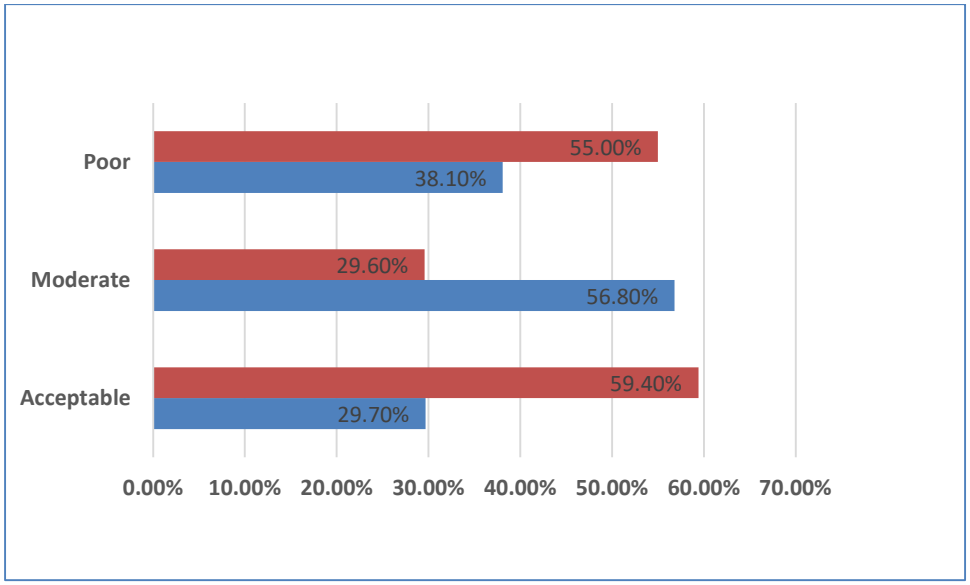

Figure 3 Participants' total Knowledge about Microbiota-gut-brain axis as a key to neuropsychiatric diseases in relation to gender

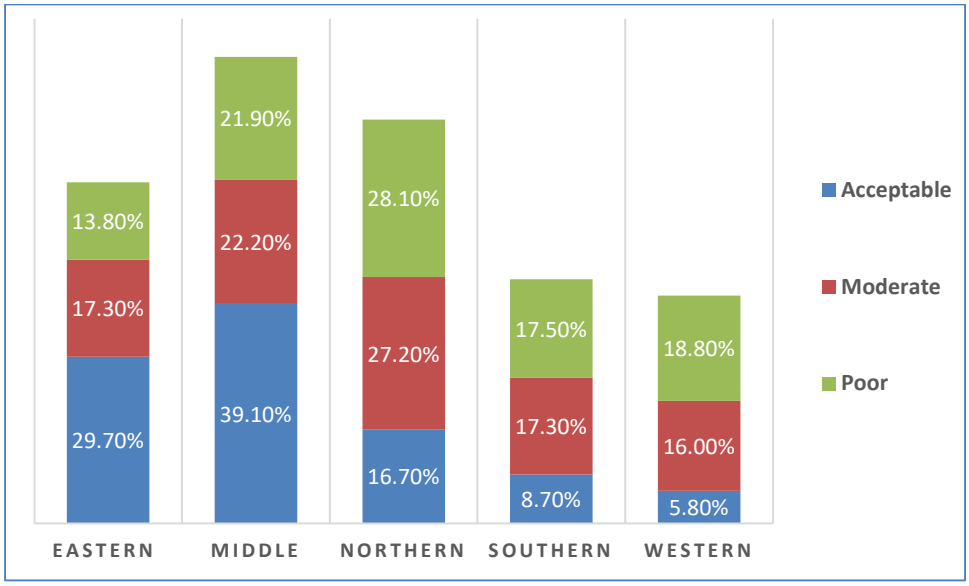

Figure 4 Participants' total Knowledge about Microbiota-gut-brain axis as a key to neuropsychiatric diseases in relation to region

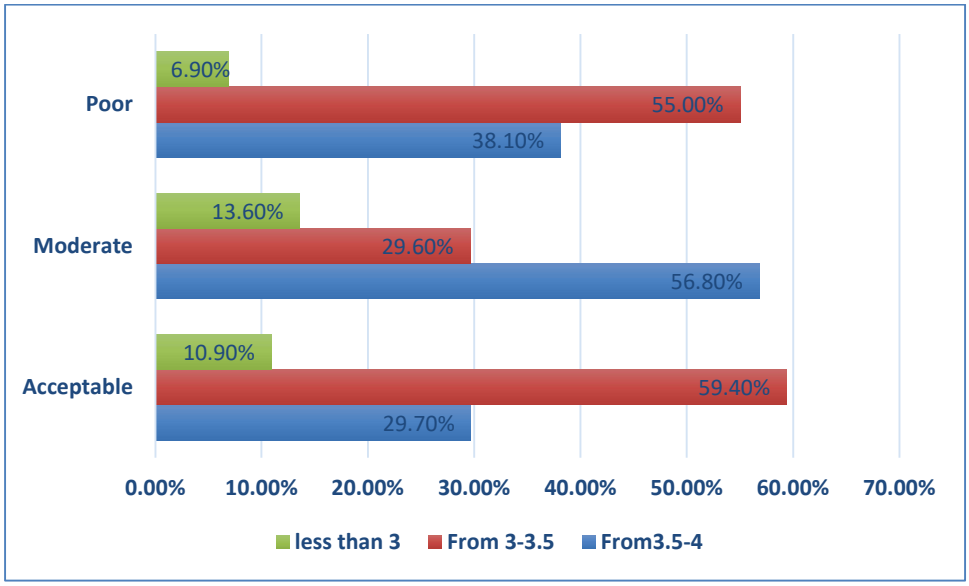

Figure 5 Participants' total Knowledge about Microbiota-gut-brain axis as a key to neuropsychiatric diseases in relation to GPA

4. DISCUSSION

Recent literature has focused on the role of microbiome in managing symptoms and restoring the physiological functions of patients suffering from different health illnesses, involving neuropsychiatric disorders. Recent Saudi research has thrown light on the role of dysbiosis in different diseases pathogenesis, however, to our knowledge; no studies have far assessed microbiome knowledge and its role in neuropsychiatric disorders. Therefore, the current study goal was to assess Saudi medical students' knowledge about human microbiota and the role of dysbiosis in the context of neuropsychiatric disorders.

The study was carried out among Saudi senior medical students and interns. The number of respondents in the questionnaire is 379, about half of them are in the fourth year, while others were in the fifth and sixth years and some are placed on their internships. Their knowledge assessment has demonstrated mixed outcomes; this can be attributed to curricular exposure and clinical practice that could potentially enhance their knowledge.

The present results reveal that our students possess adequate general knowledge about microbiota, dysbiosis and probiotics, but it could be improved further, where 35.9% have acceptable, 38% have moderate and only 26.1% have low levels of knowledge. These findings come in accordance with different studies enrolling medical students in Saudi Arabia, Jordan and Indonesia (Abu-Humaidan et al., 2021; Rahmah et al., 2021; Alamri and Al-Khater, 2022). But we observed that only 47.2% give a correct answer

when asked if there is an interaction between gut microbiota and brain, consistently with Alamri and Al-Khater, (2022) who observed low knowledge regarding microbial dynamics in various tissue compartments.

Also, the current results demonstrate that medical students lack sufficient knowledge regarding gut-brain axis and microbiome dysbiosis role in neuropsychiatric diseases pathogenesis and management. Our findings demonstrate that only 36.4% of participants have acceptable, 21.4% have moderate, whereas 42.2% have low levels of knowledge. To the best of authors' knowledge, this is the first study to assess microbiome and gut brain axis-related knowledge among Saudi medical students. Thus, these results aren't entirely comparable but coincided with earlier reports Alamri and Al-Khater, (2022), Al-Khater, (2022) and Islam et al., (2022), showing gaps in knowledge related to the role of microbiome in various health conditions among healthcare-related students and physicians. However, the present results regarding knowledge about fecal microbiota transplantation are contradictory to previous studies Madar et al., (2019) and Wu et al., (2019), reporting low level of knowledge among their participants with a medical background.

Then, we looked into the association between the knowledge level and the characteristics of studied medical students. Our study shows that female significantly have an acceptable knowledge about the role of microbiota-gut-brain axis in neuropsychiatric diseases (53.6%) comparing with 46.4% of male students (p=0.004*), indicating that female students are more interested in following the most recent information, which is in accordance with prior work reporting that female medical students were more knowledgeable than male (Elsayed-Emara et al., 2021). This observation comes in contrast to Abu-Humaidan et al., (2021) who found no significant differences in knowledge scores among male and female medical and non-medical students in Jordan.

Notably, our results reveal differences in microbiome knowledge competency among participants from different regions, those from the middle region have a significant acceptable knowledge (39.1%) about the role of microbiota-gut-brain axis in neuropsychiatric diseases in relation to other regions (p=0.00*). Also, they have higher acceptable level of knowledge about the microbiota, dysbiosis and probiotics (32.4%), but no significant differences in knowledge scores among different other regions. This could be explained by different curricular exposure as different elective courses.

Another noteworthy observation come in this study is that about half of 4th grade students (51.2%) have significant acceptable and moderate levels of knowledge (p=0.00*), which could be attributed to the course of medical research, enhancing their literature reviewing. Furthermore, students who have GPA 3.5-4 have a significant acceptable knowledge (59.4%) comparing with other students (p=0.00*).

The current findings highlight the crucial need for the development of the medical curricula to provide students with the most recent scientific information, including the role of microbiome dysbiosis in disease pathogenesis and therapeutic approaches to prevent the development of important diseases in Saudi Arabia. In addition, since learning strategies are correlated with knowledge competency level, our observations could be translated into recommendations to accommodate more modalities of learning strategies to discuss the updated scientific discoveries in different medical topics, including the microbiome, thus enhancing their knowledge acquisition.

Although, the study was conducted among medical students from different regions of Saudi Arabia which positively improve the generalizability of the results, the distribution isn't equal among gender and academic year. Moreover, this study did not evaluate students' attitudes toward probiotics.

5. CONCLUSION

This study aimed to investigate Saudi medical students' knowledge level about human microbiota and the role of dysbiosis in the context of neuropsychiatric disorders, accomplished by constructing a cross-sectional, questionnaire-based study. Overall, our study shows that our students possess adequate general knowledge about microbiota, dysbiosis and probiotics; however, it demonstrates they lack sufficient knowledge regarding gut-brain axis and microbiome dysbiosis role in neuropsychiatric diseases pathogenesis and management. Hence, developing the medical curricula, as well as, adopting more modalities of learning strategies to discuss the most recent evidence in different medical topics are crucial to enhance medical students'knowledge acquisition.

Further, another study with a larger sample size is required to validate our findings, and to assess their perception and attitude. In addition, future studies are required to investigate healthcare professionals' knowledge, perception and attitude toward microbiome in relation to neuropsychiatric diseases.

Contribution of Authors

Hemat El-Sayed El-Horany: Conceptualization of the research, Supervision of data collection, writing the manuscript; Rahaf Saleh Alenzi: Collecting data, reviewing literature; Hadeel Talal ALshammari: Sharing in collecting data, sharing in reviewing literature. Noha M Elghazally: Data analysis and revision of manuscript.

Ethical approval

The study was approved by the Research Ethics Committee (REC) of University of Hail (Ethical approval code: H-2022-379).

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Abu-Humaidan AH, Alrawabdeh JA, Theeb LS, Hamadneh YI, Omari MB. Evaluating knowledge of human microbiota among University students in Jordan, an online cross-sectional survey. Int J Environ Res Public Health 2021; 18 (24):13324. doi: 10.3390/ijerph182413324
2. Alamri A, Al-Khater SA. Evaluating the knowledge on microbiome and dysbiosis in allergic diseases among medical sciences students in Saudi Arabia. Clin Mol Allergy 2022; 20(1):2. doi: 10.1186/s12948-022-00168-x
3. Aljahdali N. The contribution of gastrointestinal microbiota in the existence of Type 2 diabetes in Saudi Arabia: Current information and perspectives. Saudi J Biol Sci 2022; 29(6):10 3286. doi: 10.1016/j.sjbs.2022.103286
4. Al-Jumah M, Bunyan R, Al-Otaibi H, Al-Towaijri G, Karim A, Al-Malik Y, Kalakatawi M, Alrajeh S, Al-Mejally M, Algahtani H. Rising prevalence of multiple sclerosis in Saudi Arabia, a descriptive study. BMC Neurol 2020; 20(1):1 -7. doi: 10.1186/s12883-020-1629-3
5. Al-Khater S. Physicians' Understanding of the Role of the Microbiome in Allergies and Asthma: A Questionnaire-Based Study in Saudi Arabia. J Asthma Allergy 2022; 15:108 1-1091. doi: 10.2147/JAA.S372725
6. Altwaijri YA, Al-Habeeb A, Al-Subaie AS, Bilal L, Al-Desouki M, Shahab MK, Hyder S, Sampson NA, King AJ, Kessler RC. Twelve-month prevalence and severity of mental disorders in the Saudi National Mental Health Survey. Int J Methods Psychiatr Res 2020; 29(3):e1831. doi: 10.1002/mpr.1831
7. Barqawi HJ, Adra SF, Ramzi HR, Abouaggour MA, Almehairi SK. Evaluating the knowledge, attitudes and practices of the UAE community on microbiota composition and the main factors affecting it: A cross-sectional study. BMJ Open 2021; 11(8):e047869. doi: 10.1136/bmjopen-2020-0 47869
8. Cattaneo A, Cattane N, Galluzzi S, Provasi S, Lopizzo N, Festari C, Ferrari C, Guerra UP, Paghera B, Muscio C, Bianchetti A, Volta GD, Turla M, Cotelli MS, Gennuso M, Prelle A, Zanetti O, Lussignoli G, Mirabile D, Bellandi D, Gentile S, Belotti G, Villani D, Harach T, Bolmont T, Padovani A, Boccardi M, Frisoni GB; INDIA-FBP Group. Association of brain amyloidosis with pro-inflammatory gut bacterial taxa and peripheral inflammation markers in cognitively impaired elderly. Neurobiol Aging 2017; 49:60-68. doi: 10.1016/j.neurobiolaging.2016.08.019
9. Cochran WG. Sampling techniques, John Wiley & Sons 1977.
10. Cowan CSM, Dinan TG, Cryan JF. Annual Research Review: Critical windows–the microbiota–gut–brain axis in neurocognitive development. J Child Psychol Psychiatry 2020; 61(3):353-371. doi: 10.1111/jcpp.13156
11. El-Metwally A, Toivola P, Al-Rashidi M, Nooruddin S, Jawed M, Al-Kanhal R, Razzak HA, Albawardi N. Epidemiology of Alzheimer's Disease and Dementia in Arab Countries: A Systematic Review. Behav Neurol 2019; 2019:3 935943. doi: 10.1155/2019/3935943
12. Elsayed-Emara H, Alhindi AA, Orebi HA, Kabbash IA, Elghazally NM. COVID-19 Pandemic: Knowledge, Attitude and Perception of Medical Students Toward the Novel

Coronavirus Disease. Disaster Med Public Health Prep 2021; 1-8. doi: 10.1017/dmp.2021.169
13. Freedman SN, Shahi SK, Mangalam AK. The gut feeling: Breaking down the role of gut microbiome in multiple sclerosis. Neurotherapeutics 2018; 15(1):109-125. doi: 10.1007/s13311-017-0588-x
14. GBD 2016 Multiple Sclerosis Collaborators. Global, regional and national burden of multiple sclerosis 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18(3):269-285. doi: 10.1016/S1474-4422(18)30443-5
15. Huang R, Wang K, Hu J. Effect of probiotics on depression: A systematic review and meta-analysis of randomized controlled trials. Nutrients 2016; 8(8):483. doi: 10.3390/nu8080483
16. Islam S, Moniruzzaman M, Biswas S, Biswas J, Arefin P, Uddin MS, Saleh MA, Zaman S. Knowledge, awareness and socio-demographic assessment of probiotics, obesity and diabetes. Inform Med Unlocked 2022; 33:101101. doi: 10.1016/j.imu.2022.101101
17. Madar PC, Petre O, Baban A, Dumitrascu DL. Medical students' perception on fecal microbiota transplantation. BMC Med Educ 2019; 19(1):368. doi: 10.1186/s12909-019-1804-7
18. Man WK, Tahirbegi B, Vrettas MD, Preet S, Ying L, Vendruscolo M, De-Simone A, Fusco G. The docking of synaptic vesicles on the presynaptic membrane induced by α-synuclein is modulated by lipid composition. Nat Commun 2021; 12(1):1-10. doi: 10.1038/s41467-021-21027-4
19. Ochoa-Repáraz J, Magori K, Kasper LH. The chicken or the egg dilemma: Intestinal dysbiosis in multiple sclerosis. Ann Transl Med 2017; 5(6):145. doi: 10.21037/atm.2017.01.18
20. Ojeda J, Ávila A, Vidal PM. Gut microbiota interaction with the central nervous system throughout life. J Clin Med 2021; 10(6):1299. doi: 10.3390/jcm10061299
21. Rahmah PA, Khairani AF, Atik N, Arisanti N, Fatimah SN. Correlation of knowledge, attitude and practice toward probiotics for the digestive system among health science students. J Multidiscip Healthc 2021; 1135-1144. doi: 10.2147/JMDH.S305670
22. Schepici G, Silvestro S, Bramanti P, Mazzon E. The Gut Microbiota in Multiple Sclerosis: An Overview of Clinical Trials. Cell Transplant 2019; 28(12):1507-1527. doi: 10.1177/0963689719873890
23. Shen T, Yue Y, He T, Huang C, Qu B, Lv W, Lai HY. The association between the gut microbiota and Parkinson's disease, a meta-analysis. Front Aging Neurosci 2021; 13:636545. doi: 10.3389/fnagi.2021.636545
24. Simpson CA, Diaz-Arteche C, Eliby D, Schwartz OS, Simmons JG, Cowan CSM. The gut microbiota in anxiety and depression – A systematic review. Clin Psychol Rev 2021; 83:101943. doi: 10.1016/j.cpr.2020.101943
25. Stopińska K, Radziwoń-Zaleska M, Domitrz I. The Microbiota-Gut-Brain Axis as a Key to Neuropsychiatric Disorders: A Mini Review. J Clin Med 2021; 10(20):4640. doi: 10.3390/jcm10204640
26. Vogt NM, Kerby RL, Dill-Mcfarland KA, Harding SJ, Merluzzi AP, Johnson SC, Carlsson CM, Asthana S, Zetterberg H, Blennow K, Bendlin BB, Rey FE. Gut microbiome alterations in Alzheimer's disease. Sci Rep 2017; 7(1):1-11. doi: 10.1038/s41598-017-13601-y
27. Włodarek D. Role of ketogenic diets in neurodegenerative diseases (Alzheimer's disease and Parkinson's disease). Nutrients 2019; 11(1):169. doi: 10.3390/nu11010169
28. Wu X, Dai M, Buch H, Bai J, Long W, Long C, Tang X, Tu H, Zhang R, Zhu C, Yang S, Cui B, Ji G, Zhang F. The recognition and attitudes of postgraduate medical students toward fecal microbiota transplantation: A questionnaire study. Therap Adv Gastroenterol 2019; 12:175628481986914 4. doi: 10.1177/1756284819869144
29. Zhu S, Jiang Y, Xu K, Cui M, Ye W, Zhao G, Jin L, Chen X. The progress of gut microbiome research related to brain disorders. J Neuroinflammation 2020; 17(1):1-20. doi: 10.1186/s12974-020-1705-z