

# Knowledge, Attitudes and Ethical and Social Perspectives Towards Fecal Microbiota Transplantation (FMT) Among Jordanian Health Care Providers

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## Research article

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# Abstract

**Background:** Fecal microbiota transplant (FMT) is a treatment modality that involves the introduction of stool from a healthy pre-screened donor into the gastrointestinal tract of a patient. It exerts its therapeutic effects by remodeling the gut microbiota and treating microbial dysbiosis-imbalance. FMT is not regulated in Jordan, and demarcating regulatory framework for FMT therapy in Jordan, an Islamic conservative country, might be faced with unique cultural, social, religious and ethical challenges. The aim is to assess knowledge, attitudes and perceptions of ethical and social issues of FMT among Jordanian healthcare professionals.

**Methods:** An observational, cross-sectional study design was used to assess knowledge, attitudes and perceptions of ethical and social issues of FMT among 300 Jordanian healthcare professionals.

**Results:** A large proportion (39%) thought that the safety and efficacy of this technique is limited and 29.3% thought there is no evidence to support its use. Among the choices to select to use FMT, almost all (95%) would only perform it in certain cases, if ethically justified, and 48.3% would use it due to treatment failure. And for reasons not to use it, 40% would not perform it due to concerns about medical litigation, followed by fear of infections (38 %), and lack knowledge of long safety and efficacy (31.3 %). Interestingly, all practitioners would perform this procedure through the lower gastrointestinal tract modality and the majority will protect patient's confidentiality via double-blinding (43.3%). For a subset of participants (n=100), the cultural constrains that might affect the choice of performing FMT were to the donor's religion, and dietary intake and alcohol consumption.

**Conclusion:** Our health care practitioners are reluctant to use the FMT modality due to religious and ethical reasons but would consider it if there was failure of other treatment and after taking into consideration many other social and ethical restrictions.

## 1. Introduction

Fecal microbiota transplant (FMT) is defined as “a procedure in which fecal matter, or stool, is collected from a tested donor, mixed with a saline or other solution, strained, and placed in a patient, by colonoscopy, endoscopy, sigmoidoscopy, or enema” (1). FMT is claimed to possess a therapeutic effect by remodeling the gut microbiota and treating microbial dysbiosis, which is often defined as an “imbalance” in the gut microbial community that is associated with disease (2-5). As such, the Infectious Diseases Society of America (IDSA) (6), Society for Healthcare Epidemiology of America (SHEA) (7) and The World Society of Emergency Surgery (WSES) (8) have recently updated the Clinical Practice Guidelines for *Clostridium difficile* Infection (CDI). The updated ISDA and SHEA guidelines include the use of FMT as a CDI treatment in the second or subsequent recurrence with strong to moderate strength of recommendation and quality of evidence (6, 7). According to Food and Drug Administration (FDA), regulation the use of FMT for recurrent CDI should clearly be explained as being an experimental approach. As such, use of FMT is a mix of clinical trial and standard of care (9).

The long history of FMT has witnessed evolution in the methodology, clinical strategies and delivery methods (10) and subsequently, updated and modernized FMT guidelines have been formulated(11-13). Parallel to its reported success in treating patients (12), the MT therapy faced and is still facing numerous regulatory, ethical, cultural and social challenges. Described ethical challenges included (14), (1)"informed consent and the vulnerability of patients"; (2)" determining what a suitable healthy donor" is; (3) "safety and risk"; (4) "commercialization and potential exploitation of vulnerable patients"; and (5) "public health implications" (14). Personal identity and family relations (15-17) have been identified as additional ethical challenges. The findings that altered microbiota can be passed to offspring (18) and the possibility of the family members, to be a potential secondary recipients, raised calls for the consideration of the ethical complexity and challenges associated with microbiome research in FMT procedures and regulations(19). Moreover due to the strong symbolic or emotive objection of certain type of diet in relation to recipient culture, religion or self-perception, Ya'arit Bokek-Cohen and Vardit Ravitsky, 2017 (20) showed that dietary intake of a stranger donor might be considered as an ethical challenge in FMT consenting procedure. All these challenges, make it very difficult to demarcate the regulatory framework (23). Indeed, the regulatory status of FMT has been changed several times and is continuously modified [21, 22].

FMT is not regulated in Jordan, and we expect that contemplating regulatory framework for FMT therapy in Jordan, with mostly a conservative Islamic tradition among its people, will definitely face unique cultural, social and religious ethical challenges.

Recently, in their paper Ma et al., 2017 (14), reported on how Chinese clinicians face social and ethical challenges associated with FMT. There is lack of understanding of these challenges in the Muslims and Arab countries and cultures.

The aim from our current study was to investigate the knowledge, attitudes and perceptions of ethical and social issues on FMT among Jordanian Health care providers to highlight the ethical challenges in the context of Jordanian's cultural and social makeup.

## **2. Methods**

### **2.1 Study design, settings, and subjects**

This was an observational, cross-sectional study design, the aim of which was to assess knowledge, attitudes and perceptions of ethical and social issues of FMT in Jordanian healthcare professionals. The study was conducted in Amman, Jordan in the period between June and August 2019. Using convenient sampling, 300 healthcare practitioners from various specialties, including physicians, laboratory technicians, and pharmacists, were invited to participate in the study and asked to fill a paper-based questionnaire. The goals of the study, as well as the questionnaire, were thoroughly explained to each participant before getting their verbal consent to participate. Their participation was voluntary and their

responses were anonymous. This study was approved by the Institutional Review Board of The Jordan University Hospital (IRB no. 80/20/9/535) dated 3/11/2019.

## 2.2 Questionnaire development

The questionnaire was adapted from a previous study by Ma *et al.* (14). The latter is distributed under the terms of the Creative Commons Attribution 4.0. International License (<http://creativecommons.org/licenses/by/4.0/>).

In brief, the questionnaire consisted of four sections comprising 20 items: general knowledge and attitudes towards FMT (four items); perception of ethical concerns (nine items); belief about social and regulatory issues (four items); and views about FMT bank ethics (three items). Question formats included single choice, multiple-choice, and written short answer. We also added questions about cultural constraints for a subset of participants (n=100).

An arbitrary negative score was created from the negative views about FMT, assigning a value of 1 for answers with negative attitude and 0 for positive attitudes. Thereafter, Independent student's t-test was used to compare the score between practitioners familiar with FMT vs. those who are not. In addition, ANOVA test was done to check the difference by profession.

## 2.3 Sample Size Calculation

For the questionnaire, sample size was calculated based on O'Rourke et al, 2013(21), where it is recommended that the number of subjects should be 5-10 times the number of items, or 100. Given that we have 21 items in our questionnaire, a sample size of 105-210 participants was considered representative for the purpose of this study.

## 2.4 Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPSS®) version 22 (SPSS® Inc., Chicago, IL, USA). The descriptive analysis was done using frequencies and percentages. Chi-square (or Fisher's) test was used to compare practitioners who were familiar and/or involved with FMT vs. those who were not. P-value less than 0.05 was considered statistically significant.

## 3. Results

Data were collected from 300 healthcare professionals. Table (1) below describes results as frequency (n) and percentage (%). Most of the participants were gastroenterologist (38%) followed by medical doctors (23.7%). The vast majority (95.7%) did not perform FMT but have heard about it.

## ***Ethics:***

Regarding ethical issues, it seems most of the responders were skeptical and not supportive of using the FMT method. A large percent (39%) thought that the safety and efficacy of this technique is limited and another 29.3% reported that there is no evidence to support its use. When asked if the methods were medically indicated and ethically approved would they use it, still only 5% would refer a patient for FMT. About 40% would not perform it due to concerns about medical litigation, followed by fear of infections (38 %), and lack knowledge of long safety and efficacy (31.3 %). But 48.3% would do it due to treatment failure and another 29.7% would do it if there was a need for organic or natural treatments.

The majority will protect patient's confidentiality via double-blinding (43.3%). Not everyone was willing to inform the patients about all risks as some would inform them about actual physical risk from the procedure and others will inform patients depending on their comprehension. With respect to the FMT bank, all participants viewed that there is a problem in donor's anonymity and data de-identification, and 47.7% were worried about the consent methods. The ethical concerns were numerous and included the mode of informed consent, privacy protection and ownership of samples.

## ***Perceptions about the use and efficacy of FMT:***

Only 20.7% believed that FMT was overrated, and more (42%) did not agree that FMT value is overrated, and the rest did not know. Interestingly, all practitioners would perform this procedure through the lower gastrointestinal rather than the upper gastrointestinal tract. A total of 43% supported the statement that FMT has negative effect on patient's dignity. As for social and regulatory issues, 87 % believed that the application of FMT should be suspended and not urgent to apply, 84 % believe that FMT will not have other future applications, and 100% said that it should not be used as the first line for CDI. Barriers to use of FMT were due to lack of guidelines (40.3%) and unknown mechanisms of action of this treatment (33.7%).

With regards to commercialization, 81.3% of participants thought that Do-it-yourself (DIY) and Direct-to-consumer (DTC) advertisement is not concerning as it is common in other areas, and 86.3% believe that FMT should not be charged for. Almost above half of them did not care about justice of allocation of benefits to the patients.

## ***Cultural aspects:***

For a subset of participants (n=100), we asked about the cultural constrains that might affect the choice of performing FMT, for 52% it was the religion, then dietary intake (25%) and alcohol consumption (23%). Due to scarce number of practitioners who fall in the category of being familiar and/or involved in FMT (13 out 300), the comparison of different variables according to this parameter would not be accurate due to large difference of sample size between these categories. However, there were results that are

worth mentioning. Those who were familiar with FMT were gastroenterologists and/or internists and only one of them did not think that it is a promising modality. All of them (n=13) would not recommend FMT due to concerns about infection, while 36.2% (n=104) of those who are not familiar FMT have such concerns (p-value=0.003). Moreover, half of those who are familiar would inform patients about physical risks vs. 16.7% in those who are not familiar with FMT informing patients about physical risks (p<0.002). Alcohol was the main cultural concern among those who did not perform FMT (25.3%), and dietary intake was the concern of those who did perform FMT (44.4% vs. 23.1%) and religion was equally concerning for both group.

Table 1  
Questionnaire items 1-20 results tabulated as frequency (n) and percentage (%).

Parameter	N	%
<b>General</b>		
<b>Profession</b>		
Gastroenterologist and/or internist	114	
	71	38.0
Medical doctor/	34	23.7
Nurse	53	11.3
Medical Laboratory technician	28	17.7
Pharmacist		9.3
<b>Familiarity with FMT</b>		
Yes, I have performed FMT	13	4.3
No, I am not familiar but I heard of it	287	95.7
No, I am not familiar nor heard of it	0	0
<b>Ethical issues</b>		
<b>What do you think of FMT?*</b>		
a) A promising treatment modality for some diseases	18	6
b) The efficacy and safety of FMT is very limited	147	39
c) The current data is not sufficient to support the use of FMT	88	29.3
d)I do not know/I am not quite sure	19	6.3
<b>If it is medically indicated and ethically approved, would you refer FMT to patient?</b>		
Yes	15	5
It depends (e.g. conventional treatment failure)	285	95
No	0	0
<b>What is/are the reason/s for you to recommend FMT and which you will also inform patients?*</b>		
a) Clinical efficacy	27	9
b) Safety	57	19
c) Failure of conventional treatment	145	48.3
	89	29.7

d) More “natural” and “organic”	19	6.3
e) Avoidance of antibiotics	81	27
f) Others.		
<b>What’s the reasons for you not to recommend FMT and which you will also inform patients?</b>		
a) Unproven treatment and unknown mechanism	81	27
b) Infections	114	38
c) Long-term risk and safety unknown	94	31.3
d) High expectation from patients puts pressure on physicians	18	6
e) Not a standard treatment, easily cause medical litigation	121	40.3
f) Others.	4	1.3
<b>Is FMT overrated (efficacy exaggerated and risk downplayed)?</b>		
Agree	62	
I do not agree	126	20.7
I do not know	112	42.0
		37.3
<b>Would you inform patients about possible risks?</b>		
I would inform about all risks	132	
I would inform about actual physical risk	55	44.0
It depends on the comprehensive ability of the patient	113	18.3
		37.7
<b>Do you think FMT has negative effect on patient’s dignity?</b>		
Agree	129	
Disagree	75	43.0
I do not know	96	25.0
		32.0
<b>What do you think is the optimal modality to deliver FMT?</b>		
Lower	300	100
Upper	0	0
<b>How to protect privacy/confidentiality?*</b>	130	43.3

a) Both donor and recipient are double-blind	41	13.7
b) Donor should be anonymized	27	9
c) Establish standardized fecal microbiota bank	89	29.7
d) FMT patients should have private ward or room	83	27.7
e) Ensure confidentiality of patient information during communication with others		
<b>Cultural constrains (only for 100 patients)</b>	52	52
Religion	25	25
Dietary intake	23	23
Alcohol consumption		
<b>Commercialization</b>		
<b>What do you think of DIY<sup>1</sup> and DTC<sup>2</sup> of FMT</b>		
Worrying	55	
It is common in other areas	244	18.3
No concerns	1	81.3
		0.3
<b>Future application (e.g. skin care)</b>		
Likely (with concerns)	48	16.0
Unlikely	252	84.0
Imaginary	0	0
<b>Social and regulatory issues of FMT</b>		
<b>Do you think it is urgent to apply FMT?</b>		
Yes urgent	39	
It should be suspended	261	13.0
		87.0
<b>Charging standard for FMT?</b>		
Yes, ASAP	41	
No need	259	13.7
		86.3
<b>FMT as first-line for CDI?</b>		

Yes	0	0
No	300	100
<b>Barriers to FMT promotion?*</b>		
	101	33.7
a) Unknown mechanism	141	13.7
b) The yuck factor and anesthetic challenges	23	7.7
c) Stained doctor-patient relationship	25	8.3
d) Lack of pharmaceutical investment	121	40.3
e) No official guidelines and regulations		
<b>Fecal microbiota bank</b>		
<b>Ethical aspect(s) concerns*</b>		
a) Informed consent mode	143	47.7
b) Privacy protection of personal information	113	37.7
c) De-identification and anonymity of donors	2	0.7
d) Ownership and property of samples	103	34.3
e) Access regulation to data and sample	57	19
f) Future use of specimen and re-contact	54	18
<b>Justice in allocation of benefits and burden</b>		
Patients should receive benefits	117	39
Patients should not	26	47
I do not care	157	52.3
1DIY: Do-It-Yourself; 2DTC: Direct-to-Consumer. *Questions were “choose all what apply” so percentages add up to more than 100%.		

Almost all the health care providers have heard of FMT but only 2% performed or were involved with this procedure. There was no significant difference in the negative views' score between practitioners familiar with FMT (n=13; mean= 9.9, SD=2.1) vs. those who are not (n=287; mean=10.3, SD=2.1); (p=0.55) (Table 2). Medical doctors had a higher negative scores than Laboratory technicians, but not statistically significant (p=0.15), and no significant differences were found between other professions, as shown in Table 2:

Table 2  
Mean negative views' score regarding FMT among different health care practitioners.

Profession	N	Mean	SD*
Gastroenterologist and/or internist	114	10.4	1.9
Medical doctor/Spec	71	10.8	1.8
Nurse	34	10.0	1.5
Medical Laboratory technician	53	9.76	1.5
Pharmacist	28	9.79	1.4
Total	300	10.2	1.8

### \*Standard Deviation

Seventy participants gave written comments about the FMT procedure. The comments were categorized into eight categories. The frequencies and percentages of participant among each category are tabulated (Table 3). The results demonstrated that a region specific, challenging dimension for the introduction and implementation of such treatment was religion. Among the participants that commented on the FMT procedure (n=70), 21 (30%) think that before introducing such a procedure a religious Fatwa or opinion is needed. Lack of experience, (24%) and cultural challenges (17%) were the other two important issues raised.

Table 3

Participants (n= 70) comments frequencies (N) and percentages (%) according to each category. Categories were arranged in descending order in relation to the number of participants in each category.

Comments Category	N	%
Needs religious Fatwa, or opinion	21	30
Lack of experience, and the need for more trials (Studies) especially in Arabic region, needs more time for evaluation	17	24
Will not fit In conservative/religious community such as Jordan or In Arabic region in general	12	17
Not acceptable (2), not effective (2), illegal (1), risky (1) or difficult to implement (2)	8	11
Limited information, lack of knowledge	4	6
Should be sought as last resort/not urgent	4	5
It might have role in future	2	3
Might be effective but should be strictly regulated and monitored	2	3

## 4. Discussion

FMT harmonized regulations are lacking and the current regulatory status ranges from non-existing to strictly regulated (22). For now, the US FDA had classified FMT as a live biotherapeutic drug that requires the submission of Investigational New Drug application for its therapeutic uses (23). CDI has been recently exempted from IND application filing, which was a decision received with high appreciation by clinicians to use FMT in a fatal ailment. Meanwhile, strict regulation and control over the use of such treatment was recommended by, Renzong Qiu, 2017 (24). He reported a concern over FMT misuse similar to stem cell treatment scenario which lately had led to a scandal in China. At that time, stem cell therapy was misused and was considered as a panacea for a multitude of clinical conditions without solid scientific evidence (24). These two different regulatory perspectives, Western versus Chinese, highlight how cross cultural differences can influence the shaping process of FMT regulations. Still, there is a gap in the understanding of FMT around the world. A study among the patients who are admitted to gastroenterology clinics in urban hospitals in California (USA) found that only 12% had knowledge what FMT is although they were receptive to the procedure itself, especially among those with college degrees (25). Interestingly, medical students attending various leading medical institution in China, also had low recognition level of FMT, that is around 48% of them did not know what FMT is (26). Accordingly, we expect that Jordan's specific social norms, tradition, customs and religion backgrounds and structures would have an impact on the attitude towards introducing and regulating FMT (24).

Our results demonstrated that the majority of the respondents heard of FMT treatment but did not practice it. In contrast to Jordan where FMT is not regulated nor practiced yet, FMT has been practiced in China since the fourth century where the traditional Chinese medicine used yellow soup, fecal slurry, orally to treat food poisoning and diarrhea (14, 27). This justifies the high familiarity of this treatment modality among Chinese clinician (14). Nevertheless, the familiarity does not guarantee experience in using it by clinicians; Zipursky, et al. (28) in their study reported that physicians have limited experience with FMT despite having treated patients with multiple recurrent CDIs.

In general, our study population were not enthusiastic about nor supportive of the introduction of such treatment. They did not see its promising utility for other future applications. Barriers towards the promotion and recommendation of FMT include mostly the absence of official guidelines and regulations followed by the risk of infections and long term risk and safety. This is in concordance with Kelly et al. (29) presentation of physicians attitudes towards FMT in 2010 at the American College of Gastroenterologist meeting. In that presentation, 40% of physicians who had heard of FMT, were not willing to try it, pending further demonstration of its efficacy safety. Nevertheless, Kelly et al., showed that physicians' recommendation was positively influenced by patients' perceived acceptance (29, 30). This was not what our respondents think. In general, unwillingness for recommending FMT treatment were previously related to many factors; the limited knowledge among the study population (31), the limited practicing numbers (32) and the "yuck" factor (33). Other reasons for physicians not offering or referring a

patient for FMT were; "not having the right clinical situation", "the belief that patients would find it too unappealing", and "institutional or logistical barriers" (28). In his commentary, Brandt et al., (33) related physicians' hesitation to recommend FMT to the limited randomized controlled trials to show effectiveness and safety. He predicted that patients' needs in addition to the availability of formulations that are aesthetically acceptable are influential parameters towards the acceptance of this treatment modality among physicians. Indeed, we reported the lower part of GI as the only acceptable route of administration of FMT. This might affect how the accepted FMT formulation to be introduced and regulated in Jordan in the future.

In support of the international legislations, our respondents will not recommend FMT as a first line treatment, but only recommend when there is failure of conventional treatment or they want organic natural treatments. This is in agreement with the Iranian clinicians and gastroenterologists attitudes who reported a willingness of accepting FMT as a therapeutic option if it is scientifically justified and ethically approved given it was used as synthetic microbiota rather than FM (34).

Clinical efficacy is a crucial factor that maintains patients' positive attitudes towards fecal microbiota transplantation (35) and physicians advising and referring patients to FMT treatment modality. The reported physicians' responses regarding the efficacy and safety of FMT were diverse. While a major concern about FMT efficacy and safety was reported among Chinese clinicians (Ma, 2017), Zipursky et al., (28) have reported minor doubts about FMT's efficacy and safety among physician respondents at Dartmouth-Hitchcock Medical Center and Baylor College of Medicine (Texas, USA).

In light of the above described barriers and limited efforts in increasing the awareness of the uses and efficacy and safety of FMT treatment modality, we predict that the introduction and the regulation of this treatment modality in Jordan is not soon.

According to the US FDA, during **the investigational use of FMT**, the potential risks and benefits including the unknown risks and the long-term risks should be clarified for qualified patients during the consenting procedure (Food and Drug Administration 2013). Consenting is an ethical challenge in FMT, which was recognized by close to 50% of our participants. The FMT consenting procedure should consider patients' vulnerability, unforeseen long term risks and limited knowledge of the actual benefits and risks to the treatment in addition to the universal ethical requirement of biomedical research (36) . Ma et al., (2017) [13] believe patients' compromised decision making capacity and vulnerability are the main challenges to informed consent. They consider CDI patients vulnerable, and desperate individuals who can be easily affected by emotive language as being natural and safe whether from physicians or the media. This was opposed by Bunnik et al., 2017(9) who believe that it is not the vulnerability or capacity to consent but rather the inadequate information that poses difficulties with regards to the FMT consenting procedure. The quality of adverse effects and risks anticipated when performing FMT is a challenging dimension in FMT procedure. Some of these are actual, as shown in the last report of FDA, (36) and others are predicted with no strong evidence, or, only examined in preclinical (i.e., animal) studies (Bunnik et al., 2017) (9). Moreover, a new risk related to the current COVID-19 pandemic has been recognized, where the

international group of experts in faecal microbiota transplantation and stool banking recently proposed the addition of SARS-CoV-2 to the current FMT donor screening measures (37). Bunnik et al., 2017 (9) highlighted that the risks of FMT may be underestimated by clinicians who are not familiar with preclinical studies. While agreeing that desperation should not be the basis for treatment decision, he demands that physicians should discuss potential long-term risks of FMT to ensure informed consent. This was appreciated by the physicians in Ma study where the majority (71% of all 100 respondents) reported they would inform patients of all known and possible risks (physical, mental, cognitive, and behavioral) and let them decide. A portion of our respondents reported that they will provide patients with all anticipated risk (44%) while 37.7% will take into consideration the comprehension capacity of the patients. This lower percentage supporting informed consent is related to poor training in ethically informed consent for clinical or research and experimental purposes.

In addition to anticipated risk, other important challenging parameters in the consenting process was highlighted by Cohen & Vardit Ravitsky (2017) (20). These were the cultural/religious or personal/ideological food restrictions (Ya'arit Bokek) of stranger donor. In their commentary, they questioned whether informed consent to FMT can be obtained without information about the donor's diet. This might be very relevant in our region. In that population of Jordan, that is mostly Muslim, observing the religious commitment to halal nonalcoholic containing foods and beverages is essential. Our respondents think that religion, dietary and alcoholic consumption will be considered as a barrier in patient's acceptance to FMT procedure. Accordingly, we perceive that it could be necessary to declare the donor's dietary habits to obtain an autonomous decision in this region.

An important parameter that was highlighted by the respondent's comments was the need to consider the religious point of view and to seek Fatwa. This was declared by 30% of the participants in addition to their perception of the need for more knowledge about safety. Therefore, we concluded that our health care practitioners are reluctant to use the FMT modality because of concerns about safety and religious beliefs (14).

Although, there is a growing awareness of ethics in human research, nevertheless Alahmad et al., 2012 have shown that research ethics regulations and guidelines in Middle Eastern Arab countries suffer from various degrees of deficiencies with regards to ethical protection (38). They recommended that social norms, tradition, customs and familial ties should all be taken into consideration when developing policies and regulations. In Interviews with medical professionals from the Middle East Alahmad et al., 2015 (39) reported the social importance of protecting confidentiality, de-identification and anonymity of donors scored 100% as being an ethical concern in conducting FMT among the Jordanian clinicians. They mostly agreed that confidentiality can be protected by double blinding both the donor and the receiver in addition to ensure the confidentiality of patient information during communication with others.

In conclusion, our study demonstrated lack of enthusiasm to implement FMT in Jordan although there is general support for its potential as a second line of treatment when traditional medical treatment fails. There are complex ethical, religious, and practice based challenges that needs to be addressed before

FMT becomes an established practice. Future studies should examine FMT from local traditional and especially religious perspectives as well as other barriers found in our study, as well as others (consenting, privacy, risks.). Patient (end-user) perspectives are lacking and would be important to understand the level of acceptability among those who need FMT. Furthermore, there should be more education to increase the understanding of FMT benefits and risks among Jordanian health care practitioners.

## **Abbreviations**

FMT: fecal microbiota transplant

IDSA: Infectious Diseases Society of America

SHEA: Society for Healthcare Epidemiology of America

WSES: World Society of Emergency Surgery

CDI: Clostridium difficile Infection

IRB: International Review Board

DIY: Do-It-Yourself

DTC: Direct-To-Consumer

SD: Standard Deviation

US FDA: The United States Food and Drug Administration

## **Declarations**

### **Ethics approval and consent to participate:**

The goals of the study, as well as the questionnaire, were thoroughly explained to each participant before getting their verbal consent to participate. Their participation was voluntary and their responses were anonymous. This study was approved by the Institutional Review Board of The Jordan University Hospital (IRB no. 80/20/9/535) dated 3/11/2019

### **Consent for publication:**

Not applicable

### **Availability of data and material:**

Available upon request

## Conflict of Interest:

None to declare

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## Authors' contributions:

Dr. AB and Dr. WA were responsible for conceptualization of this work, Dr. AB and Dr. AA planned the design (methods) and supervised data collection, Dr. AA analyzed and interpreted data. All authors were involved in writing different of parts of the manuscript as well as proof reading, therefore, they all have approved the submitted version and agreed to be accountable for their own contribution.

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## References

1. Foundation TFT. What is FMT?; 2017 [18/9/2019]. Available from: <http://thefecaltransplantfoundation.org/what-is-fecal-transplant/>.
2. Tvede M, Tinggaard M, Helms M. Rectal bacteriotherapy for recurrent Clostridium difficile-associated diarrhoea: results from a case series of 55 patients in Denmark 2000-2012. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2015;21(1):48-53.
3. Fischer M, Sipe B, Cheng YW, Phelps E, Rogers N, Sagi S, et al. Fecal microbiota transplant in severe and severe-complicated Clostridium difficile: A promising treatment approach. Gut microbes. 2017;8(3):289-302.
4. Quraishi MN, Widlak M, Bhala N, Moore D, Price M, Sharma N, et al. Systematic review with meta-analysis: the efficacy of faecal microbiota transplantation for the treatment of recurrent and refractory Clostridium difficile infection. Alimentary pharmacology & therapeutics. 2017;46(5):479-93.

5. Petrof EO, Khoruts A. From stool transplants to next-generation microbiota therapeutics. *Gastroenterology*. 2014;146(6):1573-82.
6. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2018;66(7):987-94.
7. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2018;66(7):e1-e48.
8. Sartelli M, Di Bella S, McFarland LV, Khanna S, Furuya-Kanamori L, Abuzeid N, et al. 2019 update of the WSES guidelines for management of Clostridioides (Clostridium) difficile infection in surgical patients. *World journal of emergency surgery : WJES*. 2019;14:8.
9. Bunnik EM, Aarts N, Chen LA. Physicians Must Discuss Potential Long-Term Risks of Fecal Microbiota Transplantation to Ensure Informed Consent. *The American journal of bioethics : AJOB*. 2017;17(5):61-3.
10. Zhang F, Zhang T, Zhu H, Borody TJ. Evolution of fecal microbiota transplantation in methodology and ethical issues. *Current opinion in pharmacology*. 2019;49:11-6.
11. Zhang F, Cui B, He X, Nie Y, Wu K, Fan D, et al. Microbiota transplantation: concept, methodology and strategy for its modernization. *Protein & cell*. 2018;9(5):462-73.
12. Hirsch BE, Saraiya N, Poeth K, Schwartz RM, Epstein ME, Honig G. Effectiveness of fecal-derived microbiota transfer using orally administered capsules for recurrent Clostridium difficile infection. *BMC infectious diseases*. 2015;15:191.
13. Mullish BH, Quraishi MN, Segal JP, McCune VL, Baxter M, Marsden GL, et al. The use of faecal microbiota transplant as treatment for recurrent or refractory Clostridium difficile infection and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. *The Journal of hospital infection*. 2018;100 Suppl 1:S1-S31.
14. Ma Y, Yang J, Cui B, Xu H, Xiao C, Zhang F. How Chinese clinicians face ethical and social challenges in fecal microbiota transplantation: a questionnaire study. *BMC medical ethics*. 2017;18(1):39.
15. Chuong KH, Hwang DM, Tullis DE, Waters VJ, Yau YC, Guttman DS, et al. Navigating social and ethical challenges of biobanking for human microbiome research. *BMC medical ethics*. 2017;18(1):1.
16. O'Doherty KC, Virani A, Wilcox ES. The Human Microbiome and Public Health: Social and Ethical Considerations. *American journal of public health*. 2016;106(3):414-20.
17. Metselaar S, Widdershoven G. Ethical Issues in Fecal Microbiota Transplantation: Taking Into Account Identity and Family Relations. *The American journal of bioethics : AJOB*. 2017;17(5):53-5.

18. van Opstal EJ, Bordenstein SR. MICROBIOME. Rethinking heritability of the microbiome. *Science*. 2015;349(6253):1172-3.
19. Ma Y, Chen H, Lan C, Ren J. Help, hope and hype: ethical considerations of human microbiome research and applications. *Protein & cell*. 2018;9(5):404-15.
20. Bokek-Cohen Y, Ravitsky V. Cultural and Personal Considerations in Informed Consent for Fecal Microbiota Transplantation. *The American journal of bioethics : AJOB*. 2017;17(5):55-7.
21. O'Rourke N, Psych R, Hatcher L. A step-by-step approach to using SAS for factor analysis and structural equation modeling: Sas Institute; 2013.
22. Verbeke F, Janssens Y, Wynendaele E, De Spiegeleer B. Faecal microbiota transplantation: a regulatory hurdle? *BMC gastroenterology*. 2017;17(1):128.
23. Kelly CR, Kunde SS, Khoruts A. Guidance on preparing an investigational new drug application for fecal microbiota transplantation studies. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2014;12(2):283-8.
24. Qiu R. Cross cultural perspectives on ethics and regulation of fecal microbiota for transplantation. *AME Med J*. 2017;2(88).
25. Park L, Mone A, Price JC, Tzimas D, Hirsh J, Poles MA, et al. Perceptions of fecal microbiota transplantation for *Clostridium difficile* infection: factors that predict acceptance. *Annals of gastroenterology*. 2017;30(1):83-8.
26. Wu X, Dai M, Buch H, Bai J, Long W, Long C, et al. The recognition and attitudes of postgraduate medical students toward fecal microbiota transplantation: a questionnaire study. *Therapeutic advances in gastroenterology*. 2019;12:1756284819869144.
27. Zhang F, Luo W, Shi Y, Fan Z, Ji G. Should we standardize the 1,700-year-old fecal microbiota transplantation? *The American journal of gastroenterology*. 2012;107(11):1755; author reply p -6.
28. Zipursky JS, Sidorsky TI, Freedman CA, Sidorsky MN, Kirkland KB. Physician attitudes toward the use of fecal microbiota transplantation for the treatment of recurrent *Clostridium difficile* infection. *Canadian journal of gastroenterology & hepatology*. 2014;28(6):319-24.
29. C RK, N O, L DL, D K. Barriers to greater utilization of fecal bacteriotherapy for chronic *Clostridium difficile* infection. *The American journal of gastroenterology; San Antonio, Texas, USA2010*. p. S135–S6.
30. Kelly CR, Khoruts A, Staley C, Sadowsky MJ, Abd M, Alani M, et al. Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent *Clostridium difficile* Infection: A Randomized Trial. *Annals of internal medicine*. 2016;165(9):609-16.
31. Dennis M, Salpeter MJ, Hota S. Low awareness but positive attitudes toward fecal transplantation in Ontario physicians. *The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale*. 2015;26(1):30-2.
32. Paramsothy S, Walsh AJ, Borody T, Samuel D, van den Bogaerde J, Leong RW, et al. Gastroenterologist perceptions of faecal microbiota transplantation. *World journal of gastroenterology*. 2015;21(38):10907-14.

33. Brandt LJ. Editorial commentary: fecal microbiota transplantation: patient and physician attitudes. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2012;55(12):1659-60.
34. Moossavi S, Salimzadeh H, Katoonizadeh A, Mojarrad A, Merat D, Ansari R, et al. Physicians' Knowledge and Attitude Towards Fecal Microbiota Transplant in Iran. *Middle East journal of digestive diseases*. 2015;7:155-60.
35. Xu L, Zhang T, Cui B, He Z, Xiang J, Long C, et al. Clinical efficacy maintains patients' positive attitudes toward fecal microbiota transplantation. *Medicine*. 2016;95(30):e4055.
36. U.S. Food and Drug Administration. Important Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Risk of Serious Adverse Reactions Due to Transmission of Multi-Drug Resistant Organisms: Food and Drug Administration; 2019 [updated 13/6/2019/12/2019]. Available from: <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/important-safety-alert-regarding-use-fecal-microbiota-transplantation-and-risk-serious-adverse>.
37. Ianiro G, Mullish BH, Kelly CR, Sokol H, Kassam Z, Ng SC, et al. Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel. *The lancet Gastroenterology & hepatology*. 2020;5(5):430-2.
38. Alahmad G, Al-Jumah M, Dierickx K. Review of national research ethics regulations and guidelines in Middle Eastern Arab countries. *BMC medical ethics*. 2012;13:34.
39. Alahmad G, Al Jumah M, Dierickx K. Confidentiality, informed consent, and children's participation in research involving stored tissue samples: interviews with medical professionals from the Middle East. *Narrative inquiry in bioethics*. 2015;5(1):53-66.