Pain and transition: evaluating fibromyalgia in transgender individuals

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ABSTRACT

Objective. *As members of a gender minority, transgender individuals face many challenges. Many experience distress, depression, anxiety and suicidal ideation related to gender nonconformity and transphobia.*
Stress and trauma may contribute to the development of fibromyalgia (FM) syndrome, characterised by widespread pain and fatigue. The prevalence of FM among transgenders is not known.

Methods. *Transgender participants were recruited at a specialised clinic. Questionnaires included the Widespread Pain Index (WPI), the Symptom Severity Score (SSS) and the SF-36. Data concerning hormonal treatment protocols was retrieved from charts. The current prevalence of FM was determined, as well as the prevalence before and after testosterone treatment among TM. Pearson correlations were calculated between all measures.*

Results. *115 participants were recruited, 62.6% transgender men (TM), 37.4% transgender women (TW). 17 individuals (14.8%) fulfilled the 2011 modified ACR FM criteria, for a rate of 19.4% among TM and 6.98% among TW. Among TM, FM was associated with younger age, smoking and SF-36 sub-scales related to physical functioning, role limitation due to physical pain, fatigue, pain and general health.*
Among TW, FM was associated with social status, employment, depression, existing medical treatment and substance abuse, as well as SF-36 subscales related to role limitations affected due to pain.

Conclusion. *Fibromyalgia symptoms are highly prevalent among Israeli transgender individuals and may be related to psychological distress and gender dysphoria. Healthcare professionals treating transgenders should remain vigilant for the occurrence of chronic pain, fatigue and other FM-related symptoms and be prepared to treat and/or refer such patients accordingly.*

Introduction

Transgenders are people whose gender identity differs from the sex they were assigned at birth. As members of a gender minority, transgender people face a multitude of challenges that may affect their health and wellbeing. Significant challenges are related to the experience of transphobia, manifest through both societal as well as economic discrimination (1) which may contribute to unemployment, poverty and homelessness (2-4). Many transgender people experience psychological distress related to their gender nonconformity and the discrepancy between birth sex and gender experience. The extreme form of this distress is known as gender dysphoria (5).

Research documents high prevalence of depression, anxiety and suicidal ideation among transgender individuals relative to the general population (6-8). Isolation and loneliness are also common among transgender people as a result of transphobia and rejection by loved ones (9, 10).

The world professional association of transgender health's standards of care for the health of transsexual, transgender and gender non-conforming people lists social transition, psychotherapy, surgery and hormone therapy as treatment options for individuals with gender dysphoria (11). Hormone therapy is relatively inexpensive and highly effective in the development of secondary sex characteristics. Feminising or masculinising by exogenous hormonal therapy is considered medically necessary for the transgender individuals and may relieve psychological distress associated with gender dysphoria, reduce commodities and improve patients' quality of life (11). Hormonal thera-

py protocol for transgender women (TW) generally includes dual therapy with anti-androgens (spironolactone, cyproterone acetate [CPA]) or gonadotropin releasing hormone (GnRH) agonist therapy with estrogen therapy. The hormonal therapy protocol for transgender men (TM) includes treatment with testosterone (12). This treatment is not free of adverse reactions, including cardiovascular and metabolic complications (13). Treatments such as hormone use and sex reassignment surgeries (SRS) can affect the psychological health of transgender people. For example, estrogen therapy has an emotionally calming effect on most of transgender women (13, 14). Furthermore, transgender people undergoing SRS exhibit less depression following surgery (15). On the other hand, adverse effects in terms of mental health have also been reported, including feelings of being tired and flat, tense, nervous and gloomy and depressed (16-18). Despite the above-mentioned findings, many aspects pertaining to the quality of life of transgender individuals, as well as to specific health issues, remain incompletely studied. Previous systematic reviews and meta-analyses have demonstrated low quality evidence in the existing literature (12, 19, 20). During recent decades, the trends in modern medicine have shifted towards an increased focus on quality of life and patient centred orientation. Thus, issues such as chronic pain, fatigue, and related co-morbidities, which can have a far-reaching negative impact on a patient's quality of life, as well as posing a substantial economic burden (21), have become topics of increased attention and research.

Fibromyalgia syndrome (FM), a condition characterised by chronic widespread pain and fatigue, is currently considered a prototype of centralised pain and is thought to represent centralised sensitisation (also term "pain centralisation"), *i.e.* the amplification of pain transmission and processing within the central nervous system (22). Thus, FM overlaps both clinically and pathogenetically with other complex and polygenic central nervous system disorders, such as depression (23). Moreover, similar aetiologic factors, such as stress and trauma (both physical and emotional) may contribute to the development of FM, as well as being influential in the development of such psychological comorbidities (23). These considerations point towards the clinical relevance of investigating the prevalence of FM among transgender individuals. Notably, such an association may further be hypothesised based on additional consideration, not directly related to stress. Endocrinological factors, related to hormonal treatment, are known to carry important effects on pain processing [*e.g.* the effects of estrogens (24)], and fluctuating serum hormone levels may affect pain severity (25). In addition, novel studies are currently demonstrating favourable results for the use of androgens in the treatment of centralised pain disorders (26). In view of these considerations, the aim of the current study was to evaluate the prevalence of FM among transgender individuals.

Methods

Study design

The study, performed at a specialised transgender clinic at the Tel Aviv Sourasky Medical Centre, was conducted a two-step quantitative observational research. First, a cross-sectional analysis was performed in order to estimate the prevalence of FM in the transgender population, including both transgender men (TM) and transgender women (TW). Second, a retrospective cohort study was performed in order to evaluate the prevalence of FM in TM, before and after receiving testosterone therapy. Demographic and clinical information were gathered by the use of questionnaires. The study was approved by the Institutional ethics review board and all participants gave written informed consent.

Study population

The study population included all transgender individuals treated regularly on an outpatient basis at the transgender clinic, located at the Institute of Endocrinology Metabolism and Hypertension, Tel Aviv-Sourasky Medical Centre.

Sample size

A total of 115 transgender individuals were recruited, all treated on an outpatient basis at the transgender clinic. The study population was divided into two main groups: transgender women (TW) group of 43 patients and the transgender men (TM) group of 72 patients. About 75% of the TM had data available regarding their symptoms before starting hormonal treatment (collected as part of a prior study), allowing the cohort study analysis.

Study tools

The primary research tools used were questionnaires in order to collect demographic and clinical data. In order to determine the prevalence of FM, we used the Widespread Pain Index (WPI) and Symptom Severity Score (SSS) (27). In addition, participants were asked to complete the SF-36 survey (28) in order to provide information regarding their wellbeing. Data concerning hormonal treatment protocols was retrieved from the electronic files of the study participants.

Statistical analysis

All the data was analysed using SPSS software [version 1.0.0.1347]. Statistical analysis included descriptive statistics for all measures. Pearson correlations between all measures for both study groups were calculated.

Results

115 individuals were included in this study, including 72 transgender men (62.6%) and 43 transgender women (37.4%). 17 individuals, including 14/72 (19.4%) transgender men and 3/43 (7.0%) transgender women, fulfilled 2011 modified ACR diagnostic criteria for FMS, for a total prevalence of 14.8% for the entire sample. Among transgender men, previous data was available for 54 individuals out of the total sample. 12/54 (20.7%) fulfilled ACR diagnostic criteria for FMS, prior to commencing hormonal therapy.

The demographic and clinical characteristics of the patients are presented in Table I.

Further subgroup analysis of the group of transgender men revealed a signifi-

Table I. Study participants demographics and descriptive data.

	Transgender women	Transgender men	*p*-value
Age (mean±SD)	26.9 ± 9.63	24.09 ± 6.06	0.119
Status (Relationship)	10/42 (23.8%)	23/72 (31.9%)	0.398
Work	29/43 (67.4%)	39/71 (54.9%)	0.185
Matriculation certificate	15/43 (34.9%)	50/72 (69.4%)	**0.001****
Academic degree	9/43 (20.9%)	19/72 (26.4%)	0.360
Military/National Service	5/43 (11.6%)	43/72 (59.7%)	**0.00****
Combat service	0/43 (0%)	4/71 (5.6%)	**0.045***
Medications	13/43 (30.2%)	21/72 (29.2%)	0.905
Smoking	12/43 (27.9%)	27/72 (37.5%)	0.289
Alcohol	1/43 (2.3%)	4/72 (5.5%)	0.368
Drug use	1/42 (2.3%)	0	0.323
Exercise	7/43 (16.2%)	25/72 (34.7%)	**0.021***

*p<0.05; **p<0.01.

Table II. Pearson correlation between FM prevalence and demographics and QoL parameters symptoms in the two study groups.

	Transgender women	Transgender men
WPI	**0.490****	**0.512****
SSS	**0.412****	**0.597****
Age	-0.070	-0.240*
Vitamin D***	-0.189	0.066
BMI	-0.124	-0.076
SF1 (Physical functioning)	-0.395	**-0.443****
SF2 (Role limitations due to physical pain)	**-0.440***	**-0.471****
SF3 (Role limitations due to emotional problems)	-0.298	-0.020
SF4 (Energy/fatigue)	-0.364	**-0.361***
SF5 (Emotional well-being)	-0.362	-0.127
SF6 (Social functioning)	-0.268	-0.177
SF7 (Pain)	-0.367	-0.474**
SF8 (General Health)	-0.278	**-0.512****

BMI: body mass index; SF: short form (SF-36); WPI: widespread pain index; SSS: symptom severity scale.
*p<0.05;**p<0.01. ***Vitamin D deficiency: defined as a value below 20ng/dL.

cant correlation between age and FM prevalence (spearman's rho: -0.256, p=0.030, Pearson correlation: -0.256, p=0.03). We further attempted to analyse the effect of several clinical and demographic characteristics on the presence and severity of FM symptoms. In this analysis we focused on the following parameters: components of the SF-36, representing quality of life, presence or absence of physical and mental comorbidities, BMI, medical treatment, habits, education, marital status etc. (Table II). For all parameters we compared between individuals fulfilling or not fulfilling FM criteria.

Among TM, a significant difference between individuals with and without FM was found on scores of the SF-36 questionnaire sub-scales referring to: physical functioning, role limitation affected due to physical pain, fatigue, pain and general health.

0Among TW, a significant difference was found between individuals with and without FM and the scores on the questionnaire sub-scales referring to role limitation affected due to physical pain.

In the following demographic categories, no significant difference was found in individuals with and without FM, within the TM population: being in a steady relationship (31.9%) *versus* no relationship, currently employed (54.9%) versus unemployed, educational level (69.4% 12-year education, 26.4% first degree or higher), military service (59.7% completed military or civil national service, 5.6% completed combat service).

Among TW, 10/42 (23.8%) reported being currently in a steady relationship; a significant difference was found between individuals with and without FM [χ^2 (1, n=43) =6.720, p=0.010].

29/43 (67.4%) of TW reported being currently working; a significant difference was found regarding the prevalence of FM amongst the two categories. [χ^2 (1, n= 043) =6.680, p=0.010].

24/72 (37.5%) of TM participants reported suffering from at least one of the following comorbidities: hypothyroidism, anaemia, vitamin D deficiency or obesity (Table III). χ^2 analysis demonstrated no significant difference between TM participants with and without FM regarding these comorbidities.

Among TW 6/43 (13.9%) were positive for either hypothyroidism, anaemia, vitamin D deficiency or obesity. Again, no significant difference between was found between TW participants with and without FM regarding these comorbidities.

A Pearson's correlation was performed in order to determine the relationship between BMI and FM prevalence among TM (Table III). No significant correlation was found (r= -0.006, n=69, p=0.958). Similarly, among TW, no significant correlation was found (r= -0.138, n=41, p=0.389).

23.6% of TM reported suffering from one of the following: depression, anxiety, eating disorders, post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), personality disorder, or another mental comorbidity (Table III). No significant difference in FM prevalence was found between individuals with or without any of these mental comorbidities.

11/43 (25.5%) of TW were diagnosed with one of the following: depression, anxiety, eating disorders, PTSD, ADHD, personality disorder or another mental comorbidity. Differing from the TM, in this group a significant association was evident between participants with and without FM [χ^2 (1, n=43) =9.3820, p=0.002], with a strong association found between FM prevalence and depression.

Medical treatment: 21/72 (29.2%) of TM were prescribed antidepressants, thyroidal replacements or other chronic medications. No significant difference between TM participants with and without FM was found regarding chronic treatment. On the other hand, 13/43 (30.2%) TW were found to beon

Table III. Pre-existing comorbidities (both physical and psychiatric) in both sample groups.

	Transgender women	Transgender men	*p*-value
Diseases	6/43 (13.9%)	24/72 (37.5%)	0.138
Hypothyroidism	3/43 (6.9%)	3/72 (4.2%)	0.542
Anaemia	2/43 (4.6%)	11/72 (15.3%)	0.05
Vitamin D deficiency**	13/28 (46.4%)	15/39 (38.5%)	0.699
Overweight	7/42 (16.6%)	17/72 (23.6%)	0.349
BMI (mean±SD)	23 ± 4.53	25.7 ± 6.08	**0.011***
Mental illness (frequencies detailed below)	11/43 (25.5%)	17/72 (23.6%)	0.815
Depression	8/11 (72.7%)	15/17 (88.2%)	0.773
Anxiety	5/11 (45.5%)	4/17 (23.5%)	0.285
Eating disorder	4/11 (36.3%)	1/17 (5.8%)	**0.098***
PTSD	2/11 (18.8%)	2/17 (11.7%)	0.631
ADHD	1/11 (9%)	0 (0%)	0.323
Other***	3/11 (27.2%)	7/17 (41.1%)	0.630

BMI: body mass index; PTSD: post-traumatic stress disorder; ADHD: attention deficit disorder. *$p<0.05$ **Vitamin D deficiency: defined as a value below 20ng/dL. ***Other mental illness: personality disorder or another mental comorbidity.

antidepressants, thyroidal replacements or other medications, with a significant difference between TW participants with and without FM [χ^2 (1, n= 43) =7.442, p=0.006].

Habits (smoking, alcohol, drug use, exercise): Among TM participants with and without FM, a significant difference was found only regarding smoking, [χ^2 (2, n=72) =3.996, p=0.046] whilst among TW participants a significant difference was found regarding drug-abuse and alcohol.

Comparison of FM symptoms between TM before and after hormonal treatment: For the group of TM data was obtained on first evaluation at the clinic, before initiation of hormonal treatment, and at a second visit at least one year later, after completing treatment (Table IV). No significant difference was found in WPI, SSS or total FM prevalence in this group before and after treatment. Data regarding TW was available only on a post-treatment visit (at least one year after initiating hormonal treatment). FM symptoms were found to be significantly for frequent among TM compared with TW, as shown in Table IV.

Discussion

In the current study we have demonstrated a high prevalence of fibromyalgia symptoms among the Israeli transgenders in general and in transgender men in particular, roughly six times the prevalence in the general Israeli population (29) (estimated as 2.5%) for the entire sample and almost eight times for the latter group. This key finding, which to our knowledge has not been previously reported, may shed some light on the role of both gender and psychological distress in the pathogenesis of centralised pain. Many transgender people experience severe distress**,** generally known as gender dysphoria, due to the mismatch between gender identity and sex assigned at birth. While gender dysphoria tends to ameliorate during the transition to the experienced gender (20) depression and anxiety brought upon from years of experiencing transgender-related stigma and discrimination (30, 31) remain a daily struggle. FM is considerably more prevalent in women (32) and the possibility remains that early *in utero* hormone-dependent CNS development may have a life-long effect, which could remain significant in transgender men (TM). Clearly, larger studies are required in order elucidate the aetiopathological factors underlying the higher prevalence of FM in transgender men.

Currently, the scientific community is making headway in understanding the mechanisms linking stress and chronic pain in general and FM in particular. Nonetheless, the precise role of stress among other aetiological factors awaits further elucidation (33). Like many other complex polygenic conditions, the development and severity of FM is most likely influenced by a combination of genetic susceptibility and exposure to possible triggers, including physical and emotional trauma, viral infections, exposure to chronic and acute stress, and hormonal changes (34). There are several mechanisms by which sex hormones could affect the experience of pain (35, 36). Novel studies are currently examining the role of testosterone in chronic pain conditions. Schertzinger *et al*. have demonstrated that fluctuating levels of serum testosterone may be associated with pain severity in individuals diagnosed with FM (25), while another study by Aloisi *et al*. observed a change in perception of pain in transgenders undergoing hormonal therapy (37). In our

Table IV. Prevalence of FM in sample groups.

	Transgender women	Transgender men (prior to beginning hormonal therapy)	Transgender men (after beginning of hormonal therapy)	Total study population (calculated for TW and TM after hormonal therapy)	*p*-value (calculated for TW and TM after hormonal therapy)
WPI (Mean±SD)	1.07 ± 1.83	2 ± 4.29	2.51 ± 3.89	1.97 ± 3.34	0.008**
SSS (Mean±SD)	3.19 ± 3.44	3.96 ± 3.76	5.24 ± 3.30	4.47 ± 3.48	0.002**
Fibromyalgia	3/43 (6.9%)	12/54 (22.2%)	14/72 (19.4%)	17/115 (14.8%)	0.04*

WPI: widespread pain index; SSS: symptom severity scale; TM: transgender men; TW: transgender women. *$p<0.05$; **$p<0.01$.

study, we did not find a significant difference between the prevalence of FM in the transgender men population before and after the initiation of hormonal therapy. This finding may be attributed either to the relatively short duration of treatment or to the different timing of documentation between the samples.

In the current study, we have attempted to portray and assess demographic characteristics and medical profiles of the transgender population, and to ascertain meaningful associations regarding the prevalence of FM. Interestingly, we found an inverse correlation between age and FM, that in not concurrent with the recent literature (29). This finding may be associated with the lack of a more heterogeneous sample group (selection bias), stemming from both the post-pubertal age required to commence hormonal therapy and the absence of older participants from the cohort. In addition, research indicates that younger transgender individuals before and at the beginning of the transition process, are more prone to seek self-isolation. This, in turn, keeps most youths from seeking essential mental health and medical care until crises occurs (3). Such ongoing distress might expose and aggravate existing central sensitisation syndromes such as FM (38).

Quality of life was also evaluated in the current study, with results matching past findings, demonstrating an association between the prevalence of FM and the sections of the SF-36 questionnaire covering the domains of physical functioning, role limitations due to physical pain, fatigue, pain and general health. As with other characteristics examined, inconsistencies were found between the subgroups of transgender men and women studied. This incongruity may be attributed to the smaller sample group of transgender women in the current study. We may propose, that in future quality-of-life-focused research, a spotlight should be pointed towards the change in QoL parameters during gender affirming therapy and following its aftermath. As of now, only low-quality evidence showing improvement in these parameters are present.

In conclusion, our findings highlight the increased prevalence of FM and possibly related functional disorders and symptoms, among transgender individuals and calls attention to the intriguing role of gender in the pathogenesis of chronic pain.

While the volume of research focused on this unique population is expanding, evidence regarding the influence (both physical and mental) of transitioning is scarce. Further larger-scaled research with an epidemiological, psychosocial and endocrinological point of view is called for in exploring this population. Until then, healthcare workers dealing with transgender people should be cognisant of the issues of chronic pain and related symptoms among these individuals.

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