Understanding patient-provider discordance in adolescents with lupus: The role of pain and antidepressant medication use

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Abstract
The current study examines depression and pain as potential contributors to patient-provider discordance in the assessment of lupus disease activity. The study conducted a secondary analysis of data obtained from the Childhood Arthritis and Rheumatology Research Alliance registry, with N = 859 adolescent participants. Assessments of pain, disease activity, and antidepressant medication use were collected from the patient and provider. Results indicated that depression might be underdiagnosed in pediatric lupus patients. While psychotropic medication and pain scores were independently related to greater patient-provider discordance regarding health status, pain mediated this relationship. Implications for treatment outcomes are discussed.

Keywords
adolescence, chronic illness, depression, pain, perception

Systemic Lupus Erythematosus (SLE, or lupus) is a multisystemic autoimmune disease associated with a wide spectrum of clinical manifestations and end-organ damage. Health disparities exist with greater prevalence, morbidity, and mortality for Hispanics, African-Americans, and women (Pons-Estel et al., 2010). The exact cause of lupus is unknown, the symptoms are diffuse, and the disease undergoes periods of remittance and relapse. There is no cure, definitive method of diagnosis, or standard treatment protocol.

Lupus can provide an ideal model for understanding how interactions between patients and providers impact health outcomes for adolescents with a variety of complex chronic conditions. Due to the diffuse symptoms, individuated approach to treatment, and challenges in diagnosis and treatment, patient-provider trust and communication are imperative to ongoing disease management (Bennett et al., 2011). However, discordance between provider and patient assessments of health status can have profound implications on outcomes, such as treatment adherence, expectations for improvement, and patient care (Eder et al., 2015; Yen et al., 1999). The source underlying mismatched patient-provider perceptions of disease severity has been poorly understood. Yen et al. noted that disease activity and patient quality of life for lupus patients are not always correlated as might be expected, and psychosocial risk factors associated with the disease remain an underutilized but viable explanation for sources of discordance. For example, the literature for rheumatological disorders indicates factors such as disease severity, poorer general health, greater functional disability, pain, and fatigue all increase discordance (Eder et al., 2015; Khan et al., 2012; Leong et al., 2010; Yen et al., 1999). This paper explores the value and explanatory power of psychosocial risk factors in elucidating and understanding patient-provider discordance.

Depression and other mood disorders are common “co-travelers” with lupus. There are a few reasons for high rates...
of comorbidity, such as CNS involvement, a side effect of treatment medications, or a result of living with a chronic, painful, life-threatening disease (Gupta, 2015). Studies assessing pediatric SLE patients found prevalence rates of elevated depression scores to be between 6.7% and 59%, pain was reported by 30%, and 17–20% were prescribed antidepressants (Demirkaya et al., 2008; Jones et al., 2016; Knight et al., 2016; Quilter et al., 2019). However, the literature lacks a general large sample assessment of antidepressant use and patient-provider discordance in a pediatric population.

Researchers have posited that the link between pain and depression might be explained by a shared and connected neurological pathway. For example, responses to painful stimuli are moderated by the neurotransmitters serotonin and norepinephrine, and in a state of dysregulation, these neurotransmitters may also contribute to depression (Trivedi, 2004). Karol et al. (2013) found in an adult SLE sample that those reporting moderate to severe depression also reported higher pain levels than those with no or mild depressive symptoms. Thus, pain is proposed by this study as a viable mechanism by which the relationship between depression and patient-provider discordance might be better understood.

The nature of depression and pain may manufacture pathways to discordance by creating communication gaps. In a meta-analysis examining depression as a catalyst for non-compliance, DiMatteo et al. (2000) noted that depression creates barriers to communication and treatment by hampering cognitive focus, information processing, and motivation for treatment adherence. Pain can also disrupt patient-provider communication and collaboration due to the complex, subject, and internal nature of the disorder (Frantsve and Kerns, 2007). High levels of pain tend to be underestimated and treatment efficacy overestimated on the provider side, while on the patient side mismatched treatment and outcome expectations, conflict in the assessment of etiology, and cognitive distress (e.g. catastrophizing, frustration, anger) may hinder effective communication, potentially increasing discordance (Frantsve and Kerns, 2007).

Patient-provider discordance can also be complicated by race/ethnicity as communication between the patient and provider has been found to be a source of racial disparities in healthcare. In a meta-analysis of 40 articles focused on assessing patient-provider communication in white and black patients, it was found that black patients reported more frequent problems with provider communication and information quality, and more issues concerning participation and decision-making involvement by the patient than white patients (Shen et al., 2018). This paper expands on prior research by assessing additional racial/ethnic groups and evaluates the applicability of such models for an adolescent sample, as most research has been done with adults.

Understanding factors, such as discordance, that are known contributors to medication and treatment non-adherence is especially important with a disease like lupus, as there is no defined targeted level of treatment adherence or standard medication regimen. In research examining other rheumatological disorders (i.e. Rheumatoid Arthritis) depressive symptoms were found to be the strongest independent predictor of discordance (Barton et al., 2010) but studies also indicate that depression can carry with it concomitant cognitive distortions, increased fatigue, and pain sensitivity (Trivedi, 2004). In our study, we expect greater pain and antidepressant use to be directly linked to greater discordance. Depression and pain may share neurological pathways but depression is also known to amplify pain sensation. Hence, we expect pain will be a mechanism by which depression’s relationship to discordance may be moderated or mediated. Also, it is unclear how race and gender might impact these relationships.

Methods
Participants

The data was obtained from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry. A subsample of N=859 adolescent lupus participants (ages 12–21) was pulled from data collected between 2010 and 2015 (See Table 1). This subsample data set was 17.1% male, 82.9% female, were on average 16.57 (SD = 2.26) years old, and the majority were insured. The largest categories of self-reported race/ethnicity were African American (29.6%), white (25%), Hispanic (21.3%), Asian American (11.5%), and mixed race (9.2%). Although the most frequent SES categories were <$25,000 per year (17.7%), and $25,000–$49,999 (15.1%), only 62% of the sample reported income levels.

Procedure

Participant recruitment and data collection for the registry occurred during clinical visits at pediatric rheumatology research centers in both the US and Canada. Recruitment included all current diagnosed patients with SLE. Patients filled out written informed consent and self-report measures and medical personnel filled out health, disease manifestation and progression assessments, and collected lab results. Participants were followed longitudinally every 3 months. This study addressed only the baseline data. The project follows the ethical standards of ICMJE and received institutional IRB exempt status.

Measures

Pain was assessed with a self-rated scale, ranging from 0 (i.e. no pain) to 10 (i.e. very severe pain).
**Table 1.** Descriptive statistics on study demographic variables.

| Variable                  | Percentage/ frequency/ mean |
|---------------------------|-----------------------------|
| Gender                    | 82.9% (N = 712) Female 17.1% (N = 147) Male |
| Current age               | M = 16.57 (SD = 2.26)       |
| Age at disease onset      | M = 12.93 (SD = 2.82)       |
| Income                    | 17.7% (N = 152) <$25,000 15.1% (N = 130) $25–49,999 8.7% (N = 75) $50,000–74,999 7.0% (N = 60) $75,000–99,999 7.8% (N = 67) $100,000–150,000 5.8% (N = 50) $150,000+ 37.3% (N = 320) Not reported |
| Insurance status          | 4.1% (N = 35) No insurance 92.2% (N = 792) Insured |
| Race/ethnicity            | 29.6% (N = 254) African American 25% (N = 215) White 21.3% (N = 183) Hispanic 11.5% (N = 99) Asian American 9.2% (N = 79) Mixed race 0.9% (N = 8) Race other 0.5% (N = 4) Native American |

*May not add up to 100% based on system missing values.

**Patient Disease Activity** was assessed with the Patient Global Assessment of Disease Activity (PtGA) using a self-rated scale (0-not active to 10-very active) to assess perceptions of disease activity. This tool has good psychometric properties within both adult and pediatric populations (Anderson et al., 2012).

**Physician Assessment of Disease Activity** was assessed with the Physician Global Assessment of Disease Activity (PGA) using a self-rated scale (0-not active to 10-very active). The PGA is a widely used measure of providers’ perceptions of disease activity with good psychometric properties within both adult and pediatric populations (Lattanzi et al., 2011).

**Medication history.** A questionnaire assessing medication regimen was completed by the medical provider. This study utilized only documentation of antidepressant medications (i.e. Tricyclic, SSRIs, and SNRIs).

**Results**

**Descriptive statistics**

Disorder was calculated by subtracting the provider from the patient’s ratings of disease activity level. A paired t-test of the patient’s and provider’s assessment of disease activity found adolescents rated themselves as sicker (M = 2.71, SD = 2.42) than the provider (M = 2.01, SD = 1.99; t(793) = 7.28, p < 0.001). Males (Md = 381.69) and females (Md = 399.46) did not differ on discordance scores (Mann-Whitney U = 41,604.50, p = 0.41) or use of antidepressant medication (X²(1, N = 841) = 0.004, p = 0.95), but females reported significantly more pain (Male Md = 361.75, Female Md = 431.87; Mann-Whitney U = 41,215.00, p = 0.001). One-way ANOVAs were run on discordance and pain by race/ethnicity (See Table 2). Ethnic differences were found on discordance (F(4,765) = 2.58, p = 0.04) but Tukey’s post hoc did not identify significant between-group differences at the 0.05 level. However, African American (M = 0.96, SD = 3.03) had the highest score and Asian American (M = 0.03, SD = 2.50) the lowest. Race/ethnic differences were also found on reported pain (F(4,811) = 6.85, p < 0.001). Overall African American (M = 2.93, SD = 2.81) reported significantly more pain than Caucasians (M = 2.01, SD = 2.38) and Asian American participants (M = 1.53, SD = 2.24), and Hispanic (M = 2.69, SD = 2.81) participants more than Asian Americans. A Chi-Square also found ethnic differences in antidepressant use (X²(4, N = 813) = 10.77, p = 0.03), with Caucasians (43%) reporting greater use and Asian Americans (21.2%) less use than Hispanic (20.8%), African American (25%), and mixed race (8.3%) participants.

**Prevental analyses**

Only 5.4% of the adolescents were taking/had taken antidepressant medications. A Mann-Whitney U test indicated that discordance was greater for those taking medication (Md = 478.68) compared with those not (Md = 382; U = 10,993, p < 0.007). Pain scores were positively associated with discordance (r = 0.31, p < 0.001) and were greater for those on antidepressants (Md = 513.40) than those not (Md = 404.38; U = 13,068.50, p < 0.002).

**Mediation and moderation regression analyses**

A regression and moderation/mediation analyses were conducted with discordance as the dependent variable. The regression model was significant (F(3,772) = 29.94, p < 0.001, R² = 0.11). In Step 1, pain was significant (β = 0.31, t = 8.95, p < 0.001), while antidepressant medication (dummy coded 0 = no and 1 = yes) was marginal (β = 0.07, t = 1.92, p = 0.055). In Step 2, the interaction between pain and medication use was not significant (β = -0.03, t = -0.09, p = 0.93).

Mediation procedures by Baron and Kenny (1986) were followed and graphed with the MedGraph program (Jose, 2013; see Figure 1). Antidepressant medication was a significant predictor of discordance (β = 0.11, t = 3.00, p = 0.003). Second, antidepressants were a significant predictor of pain (β = 0.13, t = 3.83, p < 0.001). Third, antidepressants were a significant predictor of discordance (β = 0.31, t = 9.29, p < 0.001). The last regression containing both medication and pain was significant (F(2,772) = 44.97, p < 0.001, R² = 0.11). Regressing pain and medication together on discordance reduced antidepressant use to marginal significance (β = 0.07, t = 1.92, p = 0.055); a
Sobel’s test indicated significant mediation ($Z = 3.52$, $p < 0.001$).

**Discussion**

The results indicated that 5.4% of the sample were prescribed antidepressant medication. The CDC notes the national prevalence rate of antidepressant use in children ages 12–19 as 3.2% (Jonas et al., 2013). However, in studies utilizing small samples or national data on lower-income participants rates of depression and pain in adolescents with lupus are highly prevalent (20–40%), as are antidepressant prescription rates (17–20%; Demirkaya et al., 2008; Jones et al., 2016; Quilter et al., 2019). While the rate of antidepressant use obtained by this study’s national sample is comparable with general youth levels, it is not comparable with adolescent lupus samples and we contend it should be considered low given the population. Demirkaya et al. (2008) also found a high percentage of participant’s depression in their pediatric SLE sample remained undetected by both pediatricians and family. This vulnerability for under-detection might occur as symptoms of depression and general mood changes thought to co-occur with adolescence are confounded.

In addition, the current study documented ethnic/racial disparities, such that African Americans self-reported more pain but Caucasians reported significantly more antidepressant use than other ethnic groups. This finding replicates prior work in this area but is not specific to lupus patients (Jonas et al., 2013; Knight et al., 2016). Lê Cook et al. (2017) found Caucasian youth had twice the antidepressant prescription rates of African Americans or Latinos and more often used psychotropics without an established prior psychological impairment. Hence, the authors deduced that Caucasians might be experiencing both increased indicated and non-indicated use. Lê Cook et al. noted that such disparities in African American and Latino medication use might be due to cultural stigma, distrust of the medical system, or restricted access to care or providers. The results of this study call for a deeper and more meaningful understanding of antidepressant medication use in youth with

Table 2. Series of one-way ANOVAs with race/ethnicity as the independent variable.

| Race/ethnicity         |       |       | F     | p     |
|------------------------|-------|-------|-------|-------|
| Hispanic               | M     | SD    |       |       |
| Caucasian              | 0.45  | 2.74  |       |       |
| African American       | 0.93  | 2.40  | 0.96  | 3.03  |
| Asian American         | 0.03  | 2.50  | 0.73  | 2.90  |
| Mixed-race             | 0.03  | 2.58  | 0.28  | 2.90  |

Table 2 shows the results of one-way ANOVAs with race/ethnicity as the independent variable. The table includes means and standard deviations for patient/provider discordance and pain scores across different ethnic groups. Means within rows with differing superscripts are significantly different at the $p < 0.05$ level based on Tukey’s post hoc paired comparisons.

**Figure 1.** Standardized regression coefficients for the relationships between antidepressant use and patient-provider discordance by pain scores. The numerical values in parentheses are beta weights taken from the second regression and the other values are zero order correlations.
lupus and to better document the mental health needs of adolescents with chronic illnesses.

Results regarding the assessment of disease activity indicated that discordance exists, with adolescents rating themselves as sicker than the provider. The literature regarding rheumatological disorders in adults demonstrated discordance between physician and patient ratings, with the patient often indicating greater disease severity, greater functional disability, and more pain and fatigue (Eder et al., 2015; Khan et al., 2012; Leong et al., 2010; Yen et al., 1999). This study provides evidence that discordance also exists in adolescent patients with lupus. However, in adolescent patients, this issue becomes even more vital as 50% of adolescents with chronic conditions are known to not comply with care recommendations, putting them at higher risk for negative outcomes and disabilities (Kyngäs et al., 2000). The current study did find evidence of racial disparities in discordance. While a post hoc test could not specify group differences, African Americans had the highest levels of discordance and Asian Americans the lowest. Integrative analysis of past research also found that African American and Hispanic patients were more likely to have less trusting relationships with their providers (Murray and McCrone, 2015). Our study provides some corroboration that these same dynamics might also exist in younger patients.

In preliminary analyses, both pain ratings and antidepressant medication use were significant predictors of discordance. Pain mediated (but did not moderate) the relationship between antidepressant use and patient-provider discordance. This would mean that the contributions of antidepressant use on discordance are explained and controlled by experiences of pain. Prior research with pediatric lupus patients found pain directly impacts reported quality of life and that pain and depression occur at high frequencies, 40% and 30% respectively (Jones et al., 2016). Researchers examining chronic diseases noted that drug therapy alone might not be enough to address health-related quality of life issues and treatments that address psychological functioning and factors, such as pain perception, pain catastrophizing, or pain-induced fear may contribute to better treatment outcomes and disease control (Jones et al., 2016; Kojima et al., 2009).

Implications

Results from this study offer healthcare providers an understanding of the need to consider psychosocial risk factors and the importance of communication and collaboration, that are key to the provider-adolescent relationship when caring for chronically ill adolescents. Neglecting to consider and/or include patients’ subjective complaints, including pain, may lead to disagreement or discordance between the provider and patients, sparking higher rates of noncompliance, loss to follow up, or refusal to follow the management plan (Levy and Signorelli, 2014). Approaching patients in a holistic manner can help promote connections with patients fostering an understanding of how chronic illnesses impact the patient’s daily lives, not just their organ systems (Watts et al., 2009). It is important for providers to understand the impact pain can have on their patient’s perceptions, communication, and compliance thus influencing their health outcomes.

In this study factors that were significantly related to the adolescent patients’ perceptions of disease status included their pain level and antidepressant medication use. While pain is a subjective measure, patients may be equally or more impacted by pain than they are with internal organ involvement. Further, it is possible that pain figures less into a provider’s calculation of overall well-being and disease status than it does for patients. For example, research with adult SLE patients found that patients tended to base their overall global assessment of disease activity on psychological status and physical status whereas physicians based their evaluation on clinical and physical findings (Stamm et al., 2007). These findings are important for providers to consider in all adolescent patients with chronic illnesses. While pain is a difficult symptom to objectively measure, it should be incorporated into the patient’s disease status level. For teens with chronic diseases the assessment must include a comprehensive evaluation of their physical, psychological, and social functioning. Identifying limitations in overall functional status, mental health, and well-being early in the disease course may help implement interventions and support services earlier to promote optimal functioning and reduce disabling impacts of the disease and/or mortality. Future research might examine how flares and remittance impact global assessments, depression, and pain and how these shifts alter the patient-provider relationship and treatment adherence over time.

Some limitations of the study were that it did not assess current disease activity. Whether the participant was in a remitting or flare stage of the disorder could impact discordance and pain ratings in a way that might be similar for other chronic diseases. Second, the CARRA data set for the years available did not contain a clinical assessment of depression, and so possible mood disorder had to be assessed indirectly through recorded antidepressant use. It also contained no indication of whether the participant was receiving therapy for depression, which might be used in conjunction with medication or without. Future research should address these issues to allow for a deeper understanding of how variables such as depression and pain impact a patient’s well-being and health outcomes. Lupus retains characteristics of many exacerbating and remitting diseases, and auto-immune diseases in particular, in that the worst symptoms and impact on pain or functioning may not be visible to the casual observer, nor always to the clinician. This paper provides evidence that lessening discordance and improving communication are factors worthy of additional investigation to benefit both providers and patients.
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Appendix

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