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A PEER-REVIEWED ARTICLE

HIV-infected adolescents have multiple risk factors for mental illness

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Since 1994, rates of perinatal transmission have dropped dramatically due to antitretroviral prophylaxis of HIV-infected pregnant women. Currently only 100-200 new cases of perinatal transmission are seen in the US annually.[1] During the same period, highly active antiretroviral therapy (HAART) has become available for pediatric patients. Perinatally-infected adolescents have been exposed to HAART and in most studies over 50% have successful viral control resulting in longer and healthier lives.[2-5] However, these adolescents have multiple risk factors for mental illness. Living with a chronic disease is associated with increased rates of mental illness and many older adolescents were infected prior to the advent of HAART and may have had a period of ineffective therapy with resultant uncontrolled viral infection in the central nervous system. Many have lost a biological parent to HIV/AIDS and may be living with another relative or foster parent. These adolescents are also frequently subjected to environments of poverty, crime, and substance abuse. Finally, many have family members with mental illness.[1,6-7]

The HIV epidemic in adolescents now includes mostly those infected through high risk behavior. Similar to the perinatally-infected adolescent, behaviorally-infected teens generally live in areas of high poverty, crime, and substance abuse. Unlike those infected perinatally, these teens usually live with a biological parent.[8] Mental illness and substance abuse rates are predicted to be high in this population since both are associated with high risk sexual behaviors.

Understanding prevalence rates and types of mental illness in both groups is important to practitioners treating HIV-infected adolescents. In HIV-infected adults, mental illness has been shown to affect adherence to antiretroviral therapy.[9] Mental illness and substance abuse in the HIV-infected adolescent may lead to poor adherence to antiretroviral therapy and risky sexual practices.

Prevalence rates for psychiatric disorders in perinatally-infected children vary depending on the type of study but generally are 55-61%. The most common disorders found are anxiety disorders (24.3-49%) followed by attention deficit hyperactivity disorders (ADHD) (14-28.6%), conduct disorders (1-12%), oppositional defiant disorders (16.7%), and mood disorders (4.3-25%).[2,6,7,9] Compared to the general population, psychiatric disorders are higher in HIV-infected children. Gaughan *et al*, in their prospective cohort study of the long-term effects of in utero and/or postnatal exposure to HIV and antiretroviral therapies (PACTG 219C), found the rates of psychiatric hospitalization in HIV-infected children 4-17 years of age to be about six times higher

than the general population with most hospitalizations for depression and behavioral disorders. No psychiatric hospitalizations were seen in the HIV-negative population.[7] Mellins *et al*, using the Diagnostic Interview Schedule for Children IV (DISC-IV) as a baseline assessment of 9-16 year old HIV-exposed youth, compared rates of psychiatric disorders in HIV-infected and HIV-seroreverters. They found higher rates of psychiatric illness in HIV-exposed children than the general population with slightly higher rates in the HIV-infected than the HIV-exposed but uninfected. The HIV-positive youth had higher rates of ADHD than the HIV-negative youth but rates of other psychiatric disorders were not significantly different between the two groups.[6] In a prospective observational study comparing HIV-infected children 6 to 17 years of age to a control group consisting of HIV-exposed and uninfected or children uninfected but living in a household with at least one HIV-infected person (IMPAACT 1055), no difference in rates of psychiatric conditions were detected by having the youth and caregivers complete the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) referenced rating scales and Child and Adolescent Symptom Inventory-4R (CASI-4R).[2]

Similar to perinatally-infected youth, youth infected through high risk behaviors also have higher rates of mental illness than the general population. Pao *et al*, using the Structured Clinical Interview for DSM-IV Axis I Disorders–Patient Edition (SCID-P), found that of the HIV-infected adolescents in their clinic, 85% had a current axis I disorder, 68% had a history of depression, and 44% currently had depression. Medical chart review revealed that 26% had a diagnosis of conduct disorder. A large percentage reported sexual and physical abuse, 50% and 38% respectively, which may partially explain the exceptionally high rates of mental illness.[8]

Risk factors for mental illness in perinatally-infected and -affected youth have been evaluated in a few studies. Traumatic life events are associated with mental illness in this population. Gaughan found that significant life events were reported three times more frequently in patients hospitalized for psychiatric illnesses.[7] HIV-associated variables such as CD4 count, CDC stage, ART use, and viral load have not been associated with having mental health disorders, but the relationship of mental illness and knowledge of HIV status varies by study.[6-7] In the study by Mellins *et al*, older youth with HIV were more likely to have behavioral disorders than younger HIV-positive youth.[6] In another study by this same group, having a mother with HIV did not increase mental health disorders in a group of HIV-negative adolescents 10-14 years of age, but knowledge of mother's HIV infection did predict worse mental health problems in this population.[10]

Substance abuse is reported in both groups of HIV-infected adolescents. Rates of substance abuse in perinatally-infected youth vary from 2% to 14%, with higher rates seen in older adolescents. Alcohol and marijuana are the most frequently abused drugs.[3,6] Williams *et al* found in their study (IMPAACT 1055) that substance abuse was associated with having other mental health disorders and lower CD4 counts. However, when compared to HIV-negative controls, HIV perinatally-infected youth did not have higher rates of substance abuse.[3] In the report by Pao *et al*, 59% of their behaviorally-

infected youth reported ever having a substance abuse problem.[8] Older adolescents are at higher risk of substance abuse, which may increase risk-taking behaviors and medication nonadherence. This could explain the association of substance abuse with lower CD4counts seen in the IMPAACT 1055 study.

HIV clinicians should therefore be aware of possible mental health problems such as anxiety disorders and ADHD in perinatally-exposed/infected youth and mood disorders in behaviorally-infected youth. Therapy for psychiatric conditions in HIV-infected youth includes both behavioral and pharmacologic therapy. Approximately 20% of HIV-infected youth are treated with psychotropic drugs and between 25-50% receive some form of behavioral intervention.[2,6,8] Psychotropic medications most frequently used include stimulants for ADHD, antidepressants, and antipsychotics for mood disorders.[11] When compared to HIV-exposed but uninfected youth, HIV perinatally-infected youth are more likely to be treated with medications and behavioral therapy for mental disorders.[2] This difference may be explained by a disparity in interaction with health care providers between HIV-positive and HIV-negative youth, although evidence to support this theory is needed. Selective serotonin uptake inhibitors (SSRIs) are the most common pharmaceutical agents used for moderate to severe depression. The FDA has issued a black box warning of a possible increased risk of suicide after starting SSRIs, however, careful evaluation of the literature does not show a clear link and should not prevent the use of these medications if needed.[12,13] Instead, careful monitoring for suicidal ideation should be practiced with all patients with a diagnosis of depression. Practitioners should also be aware of the many drug interactions that can occur between psychotropic medications and certain antiretroviral agents, antibiotics, and antifungals. Studies evaluating the efficacy of behavioral therapy in HIV-infected youth are extremely limited but suggest that group intervention may decrease stress and improve behaviors such as improved medication adherence and safe sex practices.[11]

Mental illness has been associated with poor medication adherence in adults.[9] Rudy *et al,* in a cross-sectional observational study, evaluated patient-related factors for medication adherence in HIV-infected youth 12 to 24 years of age. They found no relationship with having a mental health disorder and medication adherence. Poor adherence was associated with low self-efficacy (one's sense of being able to adhere to medications prescribed) and low outcome expectancy (one's sense of benefit from antiretroviral drugs). Greater than 50% nonadherence was seen in HIV-infected youth with low self efficacy/outcome expectancy, structural barriers, and a mental health disorder. These findings were consistent between youth infected perinatally and those infected through high risk behaviors. The only difference found between the two groups was more structural barriers related to nonadherence in the behaviorally-infected group.[4,5] It is not clear why a lack of association with poor medication adherence and a diagnosed mental health disorder in HIV-infected youth was not seen in these studies but one explanation may be high rates of treatment for mental health disorders in their study population. Based on the results of these studies, the HIV clinician should address issues

of self-efficacy, outcome expectancy, and structural barriers, in addition to treatment of mental disorders in order to maximize antiretroviral treatment adherence.

HIV-infected adolescents have very high rates of mental illness. However, several limiting factors exist in the literature. None of the studies are population-based but instead depend on samples of convenience from clinics in large metropolitan areas. This limitation may be particularly significant for behaviorally-infected youth where at least 50% may not even be diagnosed and in care.[14] Another limitation is that different researchers use different methods of evaluation of mental illness, making comparisons between studies difficult to impossible.

All of the large cross-sectional studies evaluating mental health in HIV-infected adolescents are of populations living in large metropolitan areas. Future research is needed on the mental health care needs and barriers to mental health care for HIV-infected and -affected adolescents residing in rural areas where mental health care resources are scarce.❖

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