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Psychological Manifestations of Early Childhood Adversity in the Context of Chronic Hematologic Malignancy

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Background: *Myeloproliferative neoplasms (MPNs), a group of chronic hematologic malignancies, carry significant physical and psychological symptom burdens that significantly affect patients' quality of life.* **Objectives:** *We sought to identify the relationship between early childhood adversity (ECA) and psychological distress in patients with MPNs, as ECA may compound symptom burden.* **Methods:** *Patients with MPNs were assessed for ECA (i.e., the Risky Families Questionnaire-subscales include abuse/neglect/chaotic home environment), distress (i.e., Distress Thermometer and Problem List), anxiety (i.e., Hospital Anxiety and Depression Scale-Anxiety [HADS-A]), depression (i.e., Hospital Anxiety and Depression Scale-Depression [HADS-D]), meeting standardized cutoff thresholds for distress (i.e., Distress Thermometer and Problem List* $\geq$ *4 or* $\geq$ *7)/anxiety (HADS-A* $\geq$*8)/depression (HADS-D* $\geq$ *8), and demographic factors.* **Results:** *A total of 117 participants completed the study (78% response rate). ECA was associated with depression ($p < 0.000$), anxiety ($p < 0.000$), and distress ($p < 0.000$) and problem list variables emotional ($p < 0.000$), physical ($p = 0.004$), family ($p = 0.01$), and spiritual ($p = 0.01$) by bivariate analysis and only with distress (HADS) ($p = 0.038$) on multivariate analysis. ECA was associated with meeting cutoff threshold criteria for distress ($p = 0.007$), anxiety ($p = 0.001$), and depression ($p = 0.02$). ECA subscale variables abuse and chaotic home environment were associated with psychological outcomes. ECA was higher based on disease subtypes with greater symptom burden (other > polycythemia vera > myelofibrosis > essential thrombocythemia) ($p = 0.047$) and taking an antidepressant ($p = 0.011$).* **Conclusion:** *ECA is associated with psychological distress and meets screening criteria for anxiety and depression in patients with MPNs. ECA may help to explain individual patient trajectories, and further understanding may enhance patient-centered care among patients with MPNs.*

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BACKGROUND

Distress, depression, and anxiety are highly prevalent in the context of cancer.[1–3] Unfortunately, these psychological symptoms remain underrecognized and undertreated.[4–6] The term "distress" has been accepted by the oncology community (e.g., The National Comprehensive Cancer Network [NCCC] and the American College of Surgeons) as a nonintrusive, nonstigmatizing symptom that is used to triage patients via "distress screening" to receive further diagnostic evaluation and appropriate concurrent psychological care.[7,8] Prevalence studies have documented the rates of distress, depression, and anxiety in most solid oncologic tumor types but not in the acute or chronic hematologic malignancies.[9] Similarly, descriptive studies have bolstered efforts to provide psychological services for patients with solid tumors but not in the specialized areas of acute or chronic hematologic malignancies.[10]

A recently published study highlights the high prevalence of distress, anxiety, and depression among patients with myeloproliferative neoplasms (MPNs), a chronic and progressive hematologic malignancy. This cross-sectional study found that 40% met distress-screening criteria, 31% met anxiety-screening criteria, and 12.5% met depression-screening criteria. In addition to prevalence, it is important to highlight additive risk factors for psychological sequelae in the hematologic malignancy context to proactively identify and treat these at-risk patient groups.[11,12] Understanding additional risk factors for psychological symptoms enhances the ability to meet this treatment need. However, specific vulnerability factors that help predict who is at risk to develop anxiety and depression during the cancer trajectory are not adequately described.

Psychological issues in the hematologic malignancies lead to adverse medical outcomes including prolonged hospital stay, poor adherence to treatment, and worsened quality of life.[9,13] Distress, depression, and anxiety in advanced hematologic disease are related to symptom burden and not simply related to the knowledge of an unfavorable prognosis.[1] Symptom burden and psychological issues are clearly worsened in the presence of adverse unrelenting stress, which may be explained, at least partially, by the theory of allostatic load.[14] This theory highlights the mechanism by which emotional stress leads to underlying physical changes. These biological changes are initially adaptable but become permanently irregular and dysfunctional after enduring a critical mass of stress. Similarly, early childhood adversity (ECA) predisposes patients to continual forms of stress and poor coping as an adult and is also associated with allostatic load.[15] The experience of ECA, as a vulnerability factor, primes adults to be more vulnerable to depression later in life by causing a heightened reactivity to stress.[16–18] An association in the context of chronic hematologic malignancy has not been satisfactorily studied.[19] Its elucidation may help to explain the multiple psychological trajectories that are seen after a cancer diagnoses and lack a clear explanation.[20] ECA may prime patients with MPN who are dealing with other chronic stresses (e.g., physical symptom burden) to experience psychological distress, anxiety, or depression. Although MPNs carry high physical symptom burdens that have been associated with biological markers of stress (e.g., interleukin–6 and tumor necrosis factor-alpha), which are also associated with depression and the stress theory of allostatic load, the presence of ECA may be associated with psychological symptom burden in MPNs.

The ability to identify patients who are prone to comorbid psychological symptoms at their MPN diagnosis and during treatment would help to anticipate and deliver personalized cancer care for various patient trajectories within the setting of MPN hematologic malignancy. Identifying these risk factors across many subtypes of cancer is consistent with distress screening mandates.[7]

MPNs are rare, chronic hematologic malignancies whose symptom burden often leads to impaired quality of life and inability to perform activities of daily living and have elevated rates of distress and anxiety.[21] They display a disproportionately increased symptom burden over the general population that is similar to metastatic cancer or acute myelogenous leukemia despite much-improved overall survival times lasting many years to decades in many cases.[21] Although they all carry a risk of transformation to leukemia, their symptom profiles and disease trajectories vary considerably. Worsening symptom burden is associated with worsening cytopenias (i.e., blood counts) and splenomegaly and the inability to perform activities of daily livings.[22]