

Non-pharmacological Interventions for Pediatric Cancer Patients: A Comparative Review and Emerging Needs in India

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Context: Evidence-based research on psycho-oncology in last three decades lays emphasis upon the critical role of psychological services for better illness adjustment, improved quality of life, reduced distress and cognitive problems among the rapidly increasing pediatric cancer population.

Justification: This review aims to summarize the evidence-based psychological interventions in childhood cancer over the two decades and addresses the wide gap that existed between intervention studies worldwide and India, thus highlighting the need for research and appropriate services.

Evidence acquisition: We searched electronic databases such as MedLine, PubMed, PsycINFO, and Google Scholar. Key search terms were pediatric cancer, psycho-oncology, children with cancer + psychological intervention, or multimodal treatment, psychotherapy, cognitive training, behavioral, social skills+ feasibility study, pilot, randomized controlled trial, case study, systematic reviews.

Results: 28 full papers published between 1996 to 2016, including survivors and under-treatment children below 18 years, were reviewed. Various types of key interventions were psychosocial, physical, cognitive behavioral, cognitive, music art therapy and play therapy. Generally, intervention settings were either hospital or home, and were designed to promote psychological well-being. Psychological interventions were more in customised formats in these studies. A generic intervention module was not available for replication.

Conclusion: Development of culture-specific generic intervention module and using the same in randomized control studies with larger effect size are needed in India for larger coverage of patients.

Keywords: *Counseling, Pediatric Oncology, Psychological interventions.*

The diagnosis of cancer in children and adolescents is a life-altering event for any family. In India, cancer is the ninth common cause for deaths among children aged 5 to 14 years. The proportion of childhood cancers relative to all cancers reported by Indian cancer registries varied from 0.8% to 5.8% in boys, and from 0.5% to 3.4% in girls. Leukemia and lymphoma were the commonest malignancies in boys whereas leukemia and brain tumors were commonest in girls in India [1].

The term psycho-oncology refers to diverse psychological, cognitive, social, behavioral and psychiatric factors influencing coping with cancer illness and treatment, mortality and morbidity, well-being and quality of life of survivors. Psychosocial research in pediatric psycho-oncology, a relatively recent term, began in 1960s and continued into early 1970s with predominantly observational studies of parents mourning and their psychological reaction following the death of the child or even disclosing the disease to child survivor. Subsequently, in late 1970s and early 1980s, there was increased interest in research to devise strategies to help

children undergoing treatment for cancer. In the next decade, these well-designed behavioral observational studies increased the researchers' understanding of these children's distress. Until the early 1980s, little was known about the psychological adjustment of long-term childhood cancer survivors. There was a gradual movement from case studies and clinical observations to more controlled study design and standardized psychological measurement to intervention-based randomized controlled studies targeting specific problem area in last one and half decades. In a nutshell, during the last four decades, the focus has shifted from effects of cancer on various facets of child's life to efforts of reducing the effects and improving the overall quality of life of children with cancer.

A number of studies from India have examined psychological morbidity in groups of cancer patients homogenous with respect to cancer sites [2-7]. The impact of pediatric oncology is psychosocially and physically profound [6]. However, similar to research on other pediatric chronic conditions, the majority of papers on pediatric oncology across refereed publications report

not on intervention research but on the results of descriptive and correlational research [7]. Research in psycho-oncological interventions from India is still in a nascent stage. The aim of this paper is to review the existing evidence based research in this area over the last 20 years and to highlight the gap that exists between intervention studies worldwide and India so as to highlight the need for such a study in Indian context.

PROCESS OF REVIEW

Electronic search of the articles was undertaken on Pubmed from 1996 to May 2016, to include all studies of psychological treatments for children with cancer. A search was performed using MedLine, PubMed, PsycINFO, and Google Scholar from 1996 to 2016. Retrieval of studies was done by combining key search terms such as: pediatric cancer, childhood cancer, psycho-oncology, children with cancer + psychological intervention, or multimodal treatment, psychotherapy, cognitive training, behavioral, social skills+ feasibility study, pilot, randomized controlled trial, case study, reviews. One study published in 1993 with a larger sample size which is perhaps one of the initial intervention studies in the beginning of 1990s, was also included in the review. The publications that focused on any type of non-pharmacological (predominantly psychological) intervention were included in this current review paper.

Studies published in peer-reviewed English language journals pertaining to psychological management of children with cancer were included in the present review. Titles and abstracts of all potentially relevant articles were reviewed for possible inclusion. A study was included if it was primarily a psychological/non-pharmacological intervention or the interventions focused primarily on the holistic care along with the treatment of childhood cancer, and if the study included children below 18 years' age and not with adults or parents or siblings of children with cancer, and such studies done over the past 20 years only. The articles reporting importance of psychological management or models of management were not included in the analysis.

The full texts of the identified studies were retrieved. The main outcome measure of interest was a change in the mental health profile of children with cancer (*e.g.* quality of life, behavior, sleep, fatigue, anxiety, depression, attention, academic achievement, resilience, distress etc.). Wherever data was insufficient, or not available despite contacting authors, studies were excluded from the relevant analysis. Articles describing the study protocols and dissertations were also excluded from analysis.

RESULTS

A total of 76 potentially relevant records were identified. Out of these, 31 did not meet the inclusion criteria as they were either epidemiological studies or studies on psychosocial impact or psychological morbidity. 14 studies (4 on adult patients, 4 on siblings or family members and 6 review articles) were excluded and 28 intervention studies on children with cancer were included in current analysis (one study from India) (**Fig. 1**). The characteristics of the studies and participants, results of quality assessment and key findings are described below.

Description of Studies

Details of the study design, sample and outcome has been elaborated in detail in **Web Table I**. Out of 28 studies, 18 studies were conducted on children who were under treatment and 7 studies were conducted on survivors, 2 on off-treatment patients and 1 on mixed sample. Various types of key interventions were psychosocial (7), physical (7), cognitive behavioural (4), cognitive (3), music-art therapy and play therapy (4) and other three types of intervention. One study has shown effects of mindfulness meditation and another of digital storytelling, mixed physical and psychosocial intervention has been used in one study. **Fig. 2** presents the distribution of selected studies according to their year of publication. It shows that the interest and attention towards various psychological intervention for pediatric cancer patients and survivors have been at its peak (19 out of 28 studies) in this decade, with more and more variety of studies with robust methodology being published.

Diverse range of interventions and the outcomes appear in **Table I** not only highlighted the multidimensional issues affecting the of life of pediatric cancer patients, even as survivors but also indicated a wide range of psychosocial, cognitive, behavioral, cognitive behavioral, physical (body-focused), social, and mixed types of interventions that are significant during and after the treatment. The study design and detail methodology analysis mentioned below emphasized the need to understand the technicalities so as to formulate methodologically sound interventions.

Age and gender of the participants: The lowest and the highest age at which intervention was undertaken were 12 months [9] and 216 months [14,17,20,30]. Majority of the psychological interventions have been carried out on children within the age range of 60-180 months [9,12,13,15,16,19,31-35]. Most of the studies had preponderance of males [13,17,18,19,21,22,26,31-35].

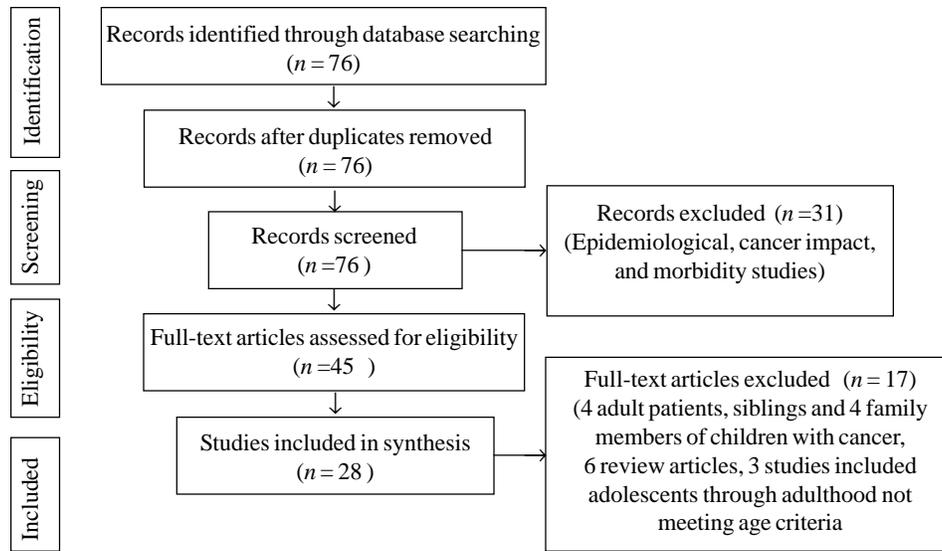


FIG. 1 Data search flowchart.

Nature of intervention

Intervention type and techniques: Evidence-based interventions for childhood cancer can be flexibly combined with other effective medical intervention approaches. These interventions represent an important component of care for children with cancer. Studies on psychological interventions in childhood cancer have supported the overall psychological health of this population while highlighting specific, cancer-related sequel that can be remediated using empirically supported interventions. The large body of research on psychological aspects of cancer, and its treatment have shown the importance for the early identification of families who may benefit from psychological intervention. Data support the use cognitive behaviour therapy specifically techniques like guided imagery, counting, breathing, awareness of feelings, thoughts, and

behavior, as well as their consequences, and to reinforce coping strategies: increasing self-awareness and self-belief; expressing positive characteristics about oneself; positive thoughts about yourself, relaxation and distraction. Overall, most of the studies reviewed here targeted improving social-emotional functioning, which might be the root cause of psychosocial distress which is highly prevalent and diverse at all stages of cancer care [36]. Many studies report the prevalence of moderate to severe post-traumatic stress among pediatric survivors [37-41] and in their families [42,43], even up to 5 years after diagnosis [37,44]. Therefore, periodic psychological assessment and including few cognitive behavioral techniques as a part of regular treatment could yield promising results.

Some of the studies have also utilized various physical techniques like aerobics, adapted physical activity, yoga, and enhanced physical exercise to manage psychological components like anxiety, sleep, cognitive fatigue and quality of life. The techniques used in these studies include self-expression through movement, fighting activities, video games, body building, walking, bike riding, dancing, pedaling a stationary bicycle-style exerciser, meditation, stretching, spinal twists, ball games, circus arts, throwing games, shooting games, racquet sports etc.

Studies demonstrating social skills interventions have targeted following social skills in order to decrease isolation and improve friendships: nonverbal communication; starting, maintaining, and ending

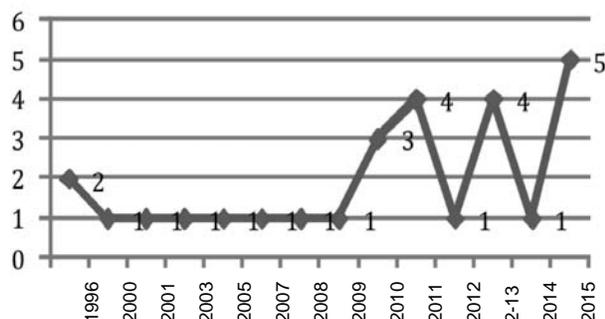


FIG. 2 Distribution of studies as per year of publication.

conversations; giving and receiving compliments; empathy and conflict resolution; and cooperation. The techniques utilized to teach these skills included a variety of fun activities and games guided by cognitive behavior strategies and expressive therapies such as music, art, and drama.

Cancer-related cognitive dysfunction refers to decline in full scale intelligence quotient (FSIQ) and/or impairment in core functional domains of attention, vigilance, working memory, executive function, processing speed, or visual motor integration [45-48]. This adversely impacts their quality of life, scholastic performance, overall personality and cognitive development. Although, in this review, cognitive interventions [16,24,25,29] primarily focused on targeted cognitive dysfunctioning/impairment, the nature of each intervention varied depending upon the targeted outcome. CogmedRM appears to be a standard computer based cognitive intervention package having moderate to high effect size, nonetheless cost could be an important factor in case of India. Hence, identification of specific problems, regular surveillance, and targeted cognitive interventions should be integrated with the regular cancer treatment programme for children who are under active treatment or for those who are survivors.

Another set of interventions included music and art therapy which focused primarily on reducing procedure-related anxiety, trauma, and increasing well-being, resilience, coping through activities like clinical dialogue, visual imagination, medical play, structured drawing, redundant reading, free drawing, dramatization, and non-directive play therapy. The techniques were applied using humanistic principles, which were mostly directed to the child and included exposure to music.

There was another type of intervention named group-based online cognitive behavioral therapy (a weekly 90-minute online group sessions for six week which is led by a psychologist, involving peer-discussion around cognitive-behavioral coping skills including: behavioral activation, thought challenging, communication and assertiveness skills training, problem-solving and goal-setting), which though excluded from the review, was found to have significant effects for adolescents >15 years and youth [49].

Frequency, number and duration of sessions: The number of sessions ranged from a minimum of two sessions to twice daily for 24 days (48 sessions). Roughly, it took 8 sessions to complete the recovery program. The vast range of sessions depended upon the nature of intervention. For example, studies with physical therapies utilized more number of sessions as

compared to cognitive behavior therapy, art therapy, social skills training or music therapy. The chief reason behind the discrepancy may be due to nature of the intervention and prime variable under study. Most of the studies utilized individualized program and individual sessions as compared to group intervention for its participants. Most of the therapy sessions were conducted once weekly each lasting for approximately 45 minutes. Overall, it took 11 to 12 weeks to complete the entire therapeutic program depending upon the nature of therapeutic module utilized.

Therapeutic outcome: The benefit of intervention has been mostly seen in anxiety and distress. Aspects of behavior (internalizing, social competence) and trauma have also been shown to improve significantly. Neurocognitive benefits have been reported for variables like attention, memory, intelligence, vigilance and learning with cognitive remediation programs. Relatively less therapeutic benefit was reported for externalizing behavior. However, it varies from studies as similar outcome variables were not included in all the studies.

Of the 28 studies included in the review, majority included a small sample and the detailed description of the methodology of intervention is missing. The training background of the professional who carried out various intervention is often not well-described in these studies. While some pilot and feasibility studies are worth studying, it is quite interesting that various forms of randomized controlled studies have also been conducted. Each study differed from the other in terms of study design, sample size, sampling, measuring tool, outcome variable, and intervention type. A wide variety of psychosocial-behavioral-play interventions are found beneficial.

In fact, coping with pediatric cancer and its treatment is a dynamic and multifaceted process that requires multiple methods of intense psychological evaluation of children and their families. Therefore, recommendations for intervention development within pediatric cancer suggest broad-based, low-cost, easily accessible cognitive-psycho-behavioral interventions that can be tailored for each family are needed [50-52].

DISCUSSION

Psychosocial interventions on pediatric cancer survivors are few but gaining attention globally [53], albeit efficacy and treatment outcomes have remained as major issues in past. Although USA tops the list of targeted psycho-oncology services to its patients, a recent study still brings out the high rate of inadequately managed services and lack of long-term surveillance in adolescent cancer survivors [54].

The scanned literature from India indicates more descriptive studies and documentation of psycho-social needs, distress, anxiety and depression mostly in adults with cancer [55-58] except one study on pediatric population [59]. Research in India has focused mainly on identifying psychosocial and psychiatric problems among the family members [60], cognitive assessment in children with acute lymphoid leukemia [61], and communicating the disease to the child [62]. The psychological manifestations included anxiety and panic (both chronic and acute), inhibited and withdrawn behavior, fear of trying new things, low emotional expressiveness, behavioral problems, high incidence of unexplained somatic complaints, intense stress, post-traumatic stress disorder, frustration and discouragement related to school difficulties, peer relationship difficulties, and loss of independence (especially during adolescence). Studies exploring psychosocial issues and management in the terminally ill as well as those on maintenance phase are fewer in number compared to those focusing on other phases of cancer trajectory (*e.g.* during active treatment of cancer survivors). The psychosocial needs identification and analysis of intra-personal processes and interpersonal dynamics in adaptation have been overlooked. In fact, interventional studies and efficacy studies are extremely few, although the positive impact of occupational therapy has been reported in last decade in India [63]. There are opportunities to further refine interventions for neurocognitive problems and to combine them with treatments that target emotional and socio-behavioural components of functioning.

Psychological intervention research, especially in pediatric psycho-oncology is lagging behind to a great extent in India. There is a need to develop and test culturally relevant intervention modules that use feasible, cost-effective modes of delivery. The role of psychological factors in survival, mechanisms of change through interventions, moderators of outcomes of interventions, comparisons of different intervention modalities, impact of psychological interventions on multiple outcomes are some of the areas within psycho-oncology which have been cited as important foci for future research worldwide [64].

The limitations of this review include lack of studies in languages other than English, and non-availability of more full text articles. Lack of homogeneity in study design and intervention has limited the review to a qualitative analysis only. While the variations in research designs and intervention outcomes provide insight into the wide range of techniques available, the limited number of studies employing each type of technique

prevented further comprehensive analysis. Hence, a definite recommendation on the most effective psychological intervention in pediatric cancer cannot be made.

Increasing number of studies highlighted the adverse impact of parental stress on pediatric survivors' emotional and somatic distress [65-67]. Therefore, reviewing studies on impact of parental interventions on child's psychosocial and behavioral functioning or even on pain management could have been worth reporting.

This is an opportune time to develop psychological interventions drawing on the relatively large literature on psychological factors and the strong tradition of clinical care provided to children with cancer by health care teams. Researchers in future can focus on developing culturally sensitive intervention module for children with cancer. They may focus on developing problem-focused techniques for children with cancer in different phases of cancer trajectory. Further, studies should also report long-term follow up of the participants in intervention. This is mainly due to the fact that childhood cancer is not only associated with apparent psychological symptoms during treatment but present themselves during post treatment in the form of neurocognitive deficits and trauma.

The review highlights a major implication for researchers to design methodologically sound studies evaluating psychological interventions in childhood cancer patients and their caregivers. Some of the research issues parallel the observations on evolution of psycho-oncology across the globe [40]. On the whole, the review of the available literature suggests that the research status in pediatric psycho-oncology in India has to witness a definite ascent while dealing with multiple challenges such as affordability of care, provision of adequate health personnel, environmental and sociocultural barriers to cancer control.

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WEB TABLE I: SUMMARY OF STUDIES INCLUDED IN THE REVIEW

<i>Study</i>	<i>Intervention components, number of participants</i>	<i>Findings</i>
<i>Social Skills Training</i>		
Varni JW, <i>et al.</i> 1993 [8]	Social skills training vs Standard school reintegration services, <i>n</i> =64	Higher perceived social support decreased internalizing/externalizing behaviours.
Die-Trill M, <i>et al.</i> 1996 [10]	Sixteen, 1 h group sessions focused on development of social skills, <i>n</i> =8	Improved social skills
Barakat LP, <i>et al.</i> 2003 [13]	Children: Social skills training: Verbal and non-verbal communication; empathy and conflict resolution; cooperation, <i>n</i> = 13	Improvement in social competence; behavior problems Better verbal and nonverbal functioning.
Barrera M, <i>et al.</i> 2009 [7]	Social skills including friendship making and assertion, <i>n</i> =32	Improved self-control, social skills, quality of life
<i>Cognitive Behavioral</i>		
Kazak AE, <i>et al.</i> 1996[9]	Distraction, play, guided imagery (customized intervention for each child), <i>n</i> =162	Lower levels of distress for the combined pharmacological + psychological intervention group
Barrera M., 2000 [11]	Two training and two in-vivo sessions, using behavioral and cognitive behavioral techniques, <i>n</i> =1	Physical resistance eliminated; maternal anxiety and sibling distress reduced
Butler WR, <i>et al.</i> 2008 [16]	22-hour individual sessions (1/wk) of Cognitive Remediation Program, <i>n</i> =161	Improved academic achievement; Less cognitive problems, better attention, less attention-hyperactivity symptoms according to parents
Hardy KK, <i>et al.</i> , 2013 [29]	25 sessions of home-based computerized cognitive training program for 3 mo, <i>n</i> =20	Improved visual working memory and reduced leaning problems
Nekah SMA, <i>et al.</i> 2015 [31]	10 sessions (60 min) of structured cognitive-behavioral group play therapy, <i>n</i> =18	Beneficial in reducing anxiety and depression
Hardy KK, <i>et al.</i> 2011 [24]	50 min/wk for 3 mo, <i>n</i> =9	Improved working memory and attention
Van Dijk-Lokkart EM, <i>et al.</i> 2015 [32]	6 + 2 sessions (children and parents respectively) of structured psychosocial program to enhance social-emotional functioning and coping, <i>n</i> =30	Overall, patients liked participation in the intervention and were positive about the psychologists
Malboeuf-Hurtubise C, <i>et al.</i> , 2013 [28]	Mindfulness meditation intervention, <i>n</i> =28	Specific outcome not mentioned
<i>Body Focused</i>		
Hinds PS, <i>et al.</i> , 2007 [15]	Pedaling a stationary bicycle-style exerciser for 30 minutes twice daily for 24 d, <i>n</i> = 29	Improved sleep
Thygeson MV, <i>et al.</i> , 2010 [18]	One 45-min session; children and parents separately and Yoga, <i>n</i> =16	Decreased anxiety in parents and adolescents
Speyer E, <i>et al.</i> , 2010 [19]	Hospital stay with APA sessions vs. hospital stay without APA session, <i>n</i> =30	Better HRQoL for most of the HRQoL psychological and physical dimensions.
Braam KI, <i>et al.</i> , 2010 [20]	Combined physical and a psychosocial intervention, <i>n</i> =100	Found to be able to maintain or enhance physical fitness and increase quality of life.
Yeh CH, <i>et al.</i> , 2011 [22]	Intervention: three weekly sessions (30minutes) of individualized home-based aerobic exercise program, <i>n</i> =22	Significantly lower “general fatigue”

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<i>Study</i>	<i>Intervention components and number of participants</i>	<i>Findings</i>
Gohar SF, <i>et al.</i> , 2011 [23]	Stretching, strengthening and aerobic exercises, <i>n</i> =9	Gross motor function and PedsQL improved steadily however, the PedsQL slightly decreased from interim maintenance to delayed intensification. The parents reported to be satisfied with the intervention.
Huang JS, <i>et al.</i> , 2014 [30]	weight management intervention (WMI), <i>n</i> =38	Less weight gain; increased moderate-to-vigorous physical activity; reduced negative mood
Vallet C, <i>et al.</i> , 2015 [34]	Adapted physical activity program, <i>n</i> =11	Improvement in global self: perceived sport competence and perceived physical strength.
Shockey DP, <i>et al.</i> , 2013 [26]	4-session of relaxation and biofeedback. Each session for 60 mins approx, <i>n</i> =11	Combination intervention found to be beneficial to children experiencing procedural distress as a novel coping strategy
<i>Music Therapy</i>		
O'Callaghan C, <i>et al.</i> , 2011 [21]	Music behaviours, <i>n</i> =26	Specific improvement not mentioned.
Polat S, <i>et al.</i> , 2015 [33]	Therapeutic music sessions (15 to 30 min) during the chemotherapy procedure, <i>n</i> =28	Reduced anxiety
<i>Others</i>		
Favara-Scacco C, <i>et al.</i> 2001 [12].	Daily psychotherapeutic encounters, <i>n</i> =32	Experimental group exhibited non-resistance and collaborative behaviors. Therapy was useful in supporting children and parents during intrusive procedures
Kazak AE, <i>et al.</i> , 2005 [14]	Pre- and 2-mo post intervention (specific techniques not mentioned), <i>n</i> =19	Reduced anxiety and parental post-traumatic stress disorder symptoms
Moore IM, <i>et al.</i> , 2012 [25]	40-50 h direct instruction on mathematical concepts, <i>n</i> =32	
Akard TF, <i>et al.</i> , 2015 [35]	Intervention that guided children to answer questions about legacy-making and create a digital story about themselves, <i>n</i> =28	Better emotional and school functioning
Chari U, <i>et al.</i> , 2013 [27]	20 sessions of non-directive play therapy. (30 min each), <i>n</i> =1	Better illness adjustment and general mental well-being, enhanced coping, and normalization.