Survival of Pediatric Leukemia: The Role of Social Determinants

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Abstract

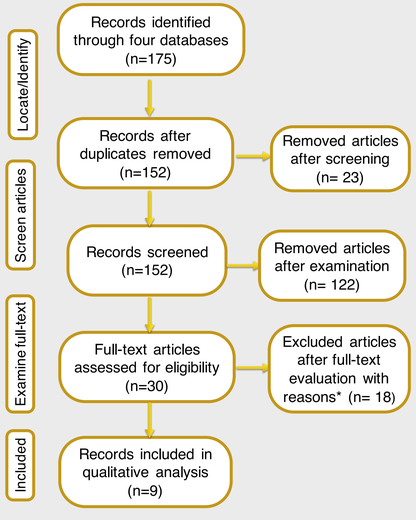
In most high-income countries, leukemia is the most common cancer in children. Currently, overall survival (OS) of children with acute leukemia is 90% in gratitude to advances in research and therapy. The goal of this structured review is to identify the association between ethnicity, social environment and survival-related outcomes of cancer treatments among children with leukemia. A search strategy was developed and applied in PubMed, EMBASE, ProQuest and Ovid (Medline) using relevant key terms related to survival related and socioeconomic factors. Electronic searches from inception to November 15th, 2017 were performed. Of the 175 publications screened for eligibility, 30 studies met the criteria for full review, and 9 studies met final inclusion criteria. The overall 5-year survival rates being reported in the studies ranged from 69.5% to 92%, with lower survival percentages coming from studies that indicate involvement of socio-demographic factors such as race and poverty. Other studies suggested no association between the survival rates as well as mortality rates and socio-demographic factors. Various studies have provided evidence and indicated that children with leukemia belonging to specific ethnic groups, and economic minority groups experience inferior survival outcomes as compared to their advantaged majority counterparts.

Introduction/ Objective

- Research has shown socioeconomic status, ethnicity/race, physical and social environment can impact overall survival rate of children with acute leukemia (Sahaja et al, 2014).
- In the adult population the association between socioeconomic factors and leukemia is clear, however that is not the case with pediatric leukemia.
- To assess *whether socio-economic factors (ethnicity and income-based factors) are associated with low survival outcomes of chemotherapy in children with leukemia?*

Methodology

Figure 1: PRISMA flow diagram[3]



*Excluded studies reported on adult populations with leukemia, duplicate publications, population-based outcomes, narrative reviews, outcome not reported by socioeconomic status and qualitative studies.
*Inclusion: studies reporting on overall, disease- free and event-free survival, and mortality: ecologic, cross section cohort, case control or RCTs.

Results

After a four step review process, 30 studies met the criteria for full review, 9 articles met inclusion criteria.

Table 1: Data quality assessment using ROBINSON-I.

Overall Moderate Risk of Bias	Overall Serious Risk of Bias
Acharya et al. (2016), Bona et al (2016), Erdmann et al. (2014), Lottick et al. (2003), Walsh & Chewning et al. (2016), Youlden et al. (2011)	Adam et al. (2016), Seif et al. (2014), Winestone et al. (2016),

Results

Table 2: Survival outcomes differ as a result of socio-demographic factors and their effect size

Author	Exposure measure	Outcome Measure	Significant	Effect size
Acharya et al. (2016)	Demographic & community income level	5 and 10 year OS	Yes	91.2% vs 69.5%
Adam et al. (2016)	Community income level	5 year mortality	No	—
Bona et al (2016)	Demographic & community income level	5 year OS	Yes	92% vs 85%
Walsh & Chewning et al. (2016)	Demographic	5 year OS	Yes	79% vs 52%
Winestone et al. (2016)	Demographic & income	Mortality	Yes	4.9% vs 1.9%
Erdmann et al. (2014)	Family Income and education	10 year OS	No	—
Seif et al. (2014)	Demographic	Mortality	No	—
Youlden et al. (2011)	Community income level	5 year OS	No *	--
Kadan-Lottick et al. (2003)	Demographic	Risk of death	Yes	80% vs 49% and 39%

*Marginally nonsignificant findings

Bias:
All studies received a moderate or serious risk of bias due to confounding variables
Strengths:
Objective measures (cancer registries) were used in all studies (low risk of bias due to measurement of outcomes)
Confounders:
- There are still potential differences in underlying tumor biology, staging, health behaviors, patients' adherence to treatment, etc.
- All studies had a low-moderate risk of bias for the rest of the domains
- Registry information data were not consistent among studies, introducing confounding factors

Study design: retrospective studies do not provide strong evidence for association
Study populations: The populations different from a random sample of pediatric cancer patients (due to missing data in the cancer registration and missing patient follow up information
Significance
More robust findings if definitions of socioeconomic status were clearly discussed

Discussion

Key Findings:

- 5/9 studies established that children with leukemia from different sociocultural backgrounds have decreased survival outcomes and consequently increased mortality rates when compared to their white counterparts (Acharya et al, 2016; Bona et al., 2016; Kadan-Lottick et al., 2003; Walsh et al., 2016; Winestone et al., 2016).
- However, results from other studies contradict socio-demographic factors to be contributing factors.

Contextualization of results:

Although many literature reviews determined a positive relationship between low socioeconomic status and inferior survival rates among pediatric leukemia, the final results remain inconsistent.

Strengths:

- Articles from different nations were analyzed to target results from high income countries.
- Selection bias was minimized because no limitation was used on the year of publication for articles that met the criteria.
- No foreign language exclusion bias.
- Another systematic review compared survival outcomes but included childhood cancers in general. Offers clear target areas for policy changes and public discussions surrounding the mechanisms of the social determinants of health.

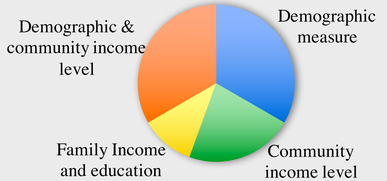
Limitations:

- The association is generalized because individual factors such as genetic differences and exposure to different hazards were not taken into consideration.

Implication for Future Research

- Future research is need to focus on specific social determinant such as SES to improve results.
- Serve as basis for interventions addressing social determinants (SDH) of health aiming to remove barriers to good health and survival outcomes.
- Paves way for future systematic literature review to examine implementation and integration of policies addressing SDH in various countries.
- Consideration of SES is important in the design of interventions as they can be a potential reason for nonadherence in socially disadvantaged families.
- Growing interest in interventions addressing SHD among children with cancer, however little information available in literature about the extent to which these interventions have been adopted in health care system.

Figure 2: Proportion of studies defining socioeconomic exposures through demographic, family income, community income or mixed measures



Conclusion

On average there is an association between social determinants and the survival outcome of childhood leukemia.
Taking limitations of the study and the mixed findings into account this relationship should be further explored.

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