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The effect of Socioeconomic ranks on the rate of Infections and Complications in the Treatment of Children's Acute Lymphoblastic Leukemia

Research article

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Abstract

Socioeconomic differences in survival among children with acute lymphoblastic leukemia (ALL) have been reported widely. However, disparities in the frequency of treatment side effects between pediatric patients from various social ranks and ethnic backgrounds have not been specifically addressed. We reviewed and collected data of 52 children diagnosed and treated for ALL in the Pediatrics Hematology and Oncology department of the hospital of south of Israel (Soroka) between 2012-2020, while comparing their demographic, ethnic, clinical characteristics, and outcomes.

Our results demonstrate that the risk of ALL was higher among the higher class of social economic rank in the south of Israel. Second, the ability to achieve complete remission among pediatric patients with ALL in the hospital of south of Israel (Soroka) was not impacted by ethnicity and social rank. Third, the number of fever episodes was higher among the higher social rank subgroup of patients, while the number of fever episodes accompanied by neutropenia and bacteremia did not vary.

These findings highlight the non-existing impact of social economic positions on patient's complications rate when set in an ideal and pro-equal health care environment, which surpasses the possible limitations of parents' income, ethnicity, and hometowns' social rank.

Key words: ALL; Socioeconomic; Children; Leukemia.

Introduction

Childhood cancers are statistically uncommon but constitute an important cause of disease and mortality in children. Specifically, acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, accounting for 25% of all pediatric oncological diseases [1,2,3]. The clinical manifestations of ALL result from unregulated proliferation of the malignant cells followed by bone marrow failure [3,4].

ALL is a multifactorial disease caused by a mix of environmental and genetic factors, which impact its incidence [5]. Past studies have demonstrated that specific environmental and genetic factors such as exposure to radiation, parents smoking, breastfeeding, kindergarten environment, house animals, and inherited diseases may increase the risk for ALL in children [6,7,8]. According to these findings, knowing environmental risk factors for childhood leukemia and adding them to the assessment of a patients' initial risk of ALL, is a vital move in the efforts to prevent and reduce ALL occurrence in childhood [5,9]. Importantly, so far, different tools to classify patients into risk groups have been established, mostly based on treatment response criteria, biological factors, patients' age and white cell count at diagnosis [10].

As a result of intense chemotherapy treatment given to ALL patients, severe adverse reactions often accompany the therapy of ALL, mainly in the shape of fever episodes. Most importantly, fever in neutropenia (FN) is both the most frequent complication of chemotherapy for cancer, and potentially deadly [11]. According to research, 50% of children treated with chemotherapy, may develop one or more FN episodes. Also, bacteremia is known to be found as an additional chemotherapy side effect in some children with FN [9,11]. Nowadays, toxicities and side effects are one of the major tasks faced by oncologists in treating ALL in children. That is due to the fact that serious adverse reactions may lead to

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therapy termination with major effects on patients' outcomes and quality of life as survivors [12].

Socioeconomic disparities in the health system are a worldwide cause of concern since socioeconomic scarcity is associated with high incidence and worse prognosis of many diseases [13]. When zooming into the incidence of ALL in childhood, data isn't concise; a recent review of early studies found that higher prevalence of ALL was associated among higher socioeconomic patients[14,15], while another review which demonstrated conflicting evidence [16]. Although the cure rates of ALL in developed countries in now nearly 90% [17], a different frequency of complications such as fever episodes, are apparent within different populations and socio-economic ranks, indicating that poorer outcomes are due to multifactorial reasons, and may be regardless of the disease or quality of treatment given [17]. Examples for these reasons could be different lifestyles, treatment termination due to financial constraints, comorbidities, and treatment-related mortality [18].

Furthermore, socioeconomic disparities in cancer survival have also been described in adult cancers throughout the world, with affluent patients showing better prognosis when compared to underprivileged patients in most cancers [17,19,20]. Studies focusing on pediatric cancer have demonstrated that socioeconomic status significantly mediates the race/ethnicity survival association for ALL, highlighting the significant influence of social and environmental factors on childhood cancer survival [15,19,21]. General socioeconomic indexes have not yet been formed, and currently most studies in the field use local indexes, such as the "Local councils and municipalities index" based on ranking and cluster membership [22]. Specifically in Israel, the variability across ethnic and racial groups was investigated recently, demonstrating how Bedouins, a highly inbred ethnic Arab population, are considered a higher risk group needing rigorous therapy and additional social support in order to improve their prognosis [23].

In our study we hypothesized that due to the equal access to healthcare in Israel, there is no correlation between a child's socioeconomic rank and ethnicity and the quantity or frequency of complications such as fever episodes accompanied by neutropenia or bacteremia, during the treatment of ALL in Israeli hospitals. We reviewed and collected data of 52 children diagnosed and treated for ALL in the hospital of south of Israel (Soroka), while comparing their demographic, ethnic, clinical characteristics, and outcomes.

Materials and Methods

Cohort and Data Collection

In the following retrospective population-based cohort study, data of all pediatric patients with the diagnosis of ALL, admitted and treated in the Pediatrics Hematology and Oncology department of the hospital of south of Israel (Soroka) between 2012-2020 was collected manually from the Chameleon EMR [24] Medical data base, and statistically analyzed. The Chameleon EMR documents the patient's clinical journey from admin to discharge creating complete electronic medical records. The following parameters were collected from the Chameleon EMR medical data base: lab parameters including CBC (haemoglobin, neutrophils, white blood cells, albumin, c-reactive protein) and pathology reports (Immunophenotype, CNS status, risk of ALL), demographic information (age, ethnicity, gender, BMI) and manual count of hospitalizations during treatment protocol.

Inclusion Criteria

Inclusion criteria included all patients under the age of 18 at diagnosis, from all levels of risk of ALL, who completed a 2-year course of chemotherapy treatment, were diagnosed between 2012-2020 and were known to the participating social worker in the study. Patients who had a change of diagnosis, or no computerized data records were excluded from the study. The study population includes 52 ALL patients; 26 Jewish and 26 Bedouin, demographics are shown in table 1, and a flowchart is shown in figure 1.

Table-1: Characteristics of the cohort of pediatric ALL children treated in the hospital of south of Israel (Soroka) between 2010-2020.

	Number (percentage)
Social Rank	
Low n(%)	22(41.5%)
Medium/High n(%)	30(58.5%)
Ethnicity	
Jewish n(%)	26(50.0%)
Bedouin n(%)	26(50.0%)
Gender	
Male n(%)	30(58.5%)
Female n(%)	22(41.5%)
BMI	
Mean ± SD	17.33+/-3.54
Age (Years)	
Mean ± SD	7+/-5.14
Local Counsils and Municipalities Socioeconomic index	
Mean ± SD	-0.64+/-1.17
Immunophenotype	
B cell n(%)	42(81.1%)
T cell n(%)	9(17.0%)
B+T cell n(%)	1(1.9%)
CNS Status	
Mean ± SD	4.42+/-30.20
Hemoglobin	
Mean ± SD	7.24+/-2.69
Neutrophils	
Mean ± SD	1.12+/-1.29
WBC	
Mean ± SD	13.82+/-24.15
Albumin	
Mean ± SD	3.59+/-0.54
CRP	
Mean ± SD	38.25+/-57.56
Failed to achieve complete remission	
No n (%)	14 (31.1%)
Yes n(%)	31 (68.9%)
Risk of ALL	
Standard n(%)	46 (88.7%)
High n(%)	6 (11.3%)
Number of fever episodes	
Mean ± SD	7.60+/-5.49
Number of fever episodes and Neutropenia	
Mean ± SD	2.89+/-2.37
Number of fever episodes and Neutropenia and Bacteremia	
Mean ± SD	0.49+/-0.89

The frequencies and percentages of the nominal and dichotomous variables were presented. Continuous variables were described and represented by the mean and the standard deviation or by the median and the range of the values.

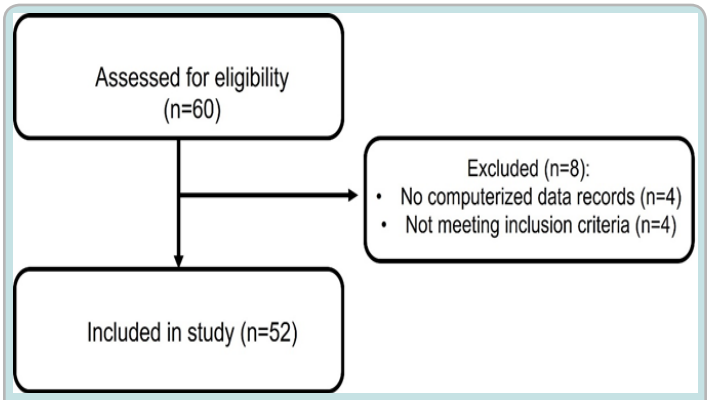

Figure 1: Inclusion flowchart in a study cohort of children diagnosed with Acute Lymphoblastic Leukemia (ALL) diagnosed during 2012–2019, Soroka, Israel.

Tested Variables

The variable "Social rank" was defined by a socioeconomic status evaluation performed by social workers of the Pediatric Hemato-oncologic Unit in the hospital of south of Israel (Soroka). These Social workers are familiar with the specific cases and patients chosen for the study, and their evaluation was based on patients' ethnicity, living condition (private house, apartment buildings, tents, etc.), parents' income, education, and lifestyle. This variable is not necessarily specific nor objective and is solely based on the information provided by patients' parents to the social workers of the Pediatric Hemato-oncologic Unit in the hospital of south of Israel (Soroka). The variable "Social rank" split patients into two subgroup- Low and Medium/High. The variable "Local councils and municipalities index" is based on the Israeli local councils and municipalities by socio-economic index- ranking and cluster membership [22]. The range of this continuous variable is -2 to 2.5. Importantly, this variable, which demonstrates the patient's sociodemographic background, was not used in the social workers' estimation of the "Social rank". The Variable "Risk of ALL" divided patients to either High or Low risk based on past studies [3], according to both: genetic factors in the form of polymorphic variants in several genes (including ARID5B, CEBPE, GATA3, and IKZF1), and exposure to radiation and certain chemicals in the past.

The Variable "Failure to achieve complete remission" divided patients into two groups based on their ability to achieve complete remission after a 2-year chemotherapy treatment.

Statistical Analysis

The statistical analysis was preformed using SAS software (release 9.04). The results were considered significant when the p value was less than 0.05.

Descriptive Statistics

The frequencies and percentages of the nominal and dichotomous variables are presented separately for the two Ethnicity groups (Jews and Bedouins). Normally distributed continuous variables are described and represented by the mean and standard deviation and non-normally distributed continuous variables are described and represented by the median and the interquartile range.

Univariate Analysis

The Fishers Exact Test was used to determine the relation between the categorial independent variables and the dichotomous outcome variable (failed to achieve complete remission, Risk of ALL). The relation between the continuous variables and the dichotomous outcome variable (failed to achieve complete remission, Risk of ALL) was examined using the logistic regression. The relation between the independent variables and the Count outcome variables (Number of fever episodes, Number of fever episodes+ Neutropenia, Number of fever episodes+ Neutropenia+ Bacteremia) was examined using the Poisson regression. A Poisson regression was conducted to compare the effect of the categorical variables on the count variable (Number of fever episodes). The relation between the continuous independent variables and the continuous outcome variable (Number of fever episodes, Number of fever episodes+ Neutropenia, Number of fever episodes+ Neutropenia+ Bacteremia) was examined using the Pearson's correlation coefficient.

Bivariate Analysis

The relationship between each of the independent variables, the socioeconomic status, and the dichotomous dependent variables (failure to achieve complete remission and Risk of ALL) was examined using a Logistic regression model. The relationship between each of the independent variables, the socioeconomic status, and the Count outcome variables (Number of fever episodes, Number of fever episodes+ Neutropenia, Number of fever episodes+ Neutropenia+ Bacteremia) was examined using a Poisson regression models.

Multivariate Analysis

Logistics regression analysis was used to determine the association between the independent variables and the dichotomous outcomes (failure to achieve complete remission). Poisson regression analysis was used to investigate the association between the independent variables and the Count outcome variables (Number of fever episodes, Number of fever episodes+ Neutropenia, Number of fever episodes+ Neutropenia+ Bacteremia). Variables to be found significant in the univariate and bivariate analysis entered the model.

Results

In the following study, data of all pediatric patients with the diagnosis of ALL, admitted and treated in the Pediatrics Hematology and Oncology department of the hospital of the south of Israel (Soroka) between 2012-2020 was collected and analyzed. The study population includes 52 ALL patients; 22 Low social rank and 31 medium-high social rank, demographics are shown in table 1.

Risk of ALL

First, we aimed to determine whether a variety of demographic and clinical parameters of patients during their initial admission to the hospital, have an impact on their risk of ALL. We found a significant relation between higher social ranks and a higher risk of ALL (n=52, p=0.0033) with 27% of Medium/High social ranked patients (n=6) being considered high risk of ALL, and 100% of low social rank (n=31) considered standard risk of ALL (figure 2A). Additionally, as shown in figure 2C, a significant relation between the risk of ALL and the local councils and municipalities socioeconomic index of patients was found (n=52, p=0.03), meaning with every increase by 1 point in the local councils and municipalities socioeconomic index, there is a 0.31 increase in the risk for ALL. Furthermore, lab parameters also correlated with patients' risk of ALL and showed a significant relation with

Immunophenotype (n=52, p=0.01), where 100% of patients with a B+T cell Immunophenotype were found with higher risk of ALL (figure 2B). Also, a significant relation between the risk of ALL and WBC levels of patients at admission was found (n=52, p=0.01), where higher WBC increase the odds for high risk of ALL. When examining this question through a bivariate analysis using a logistic regression model, we found no significant connections between the listed independent variables, the patients' social rank, and their risk stratification for ALL, insinuating social rank's minor role in the occurrence of ALL.

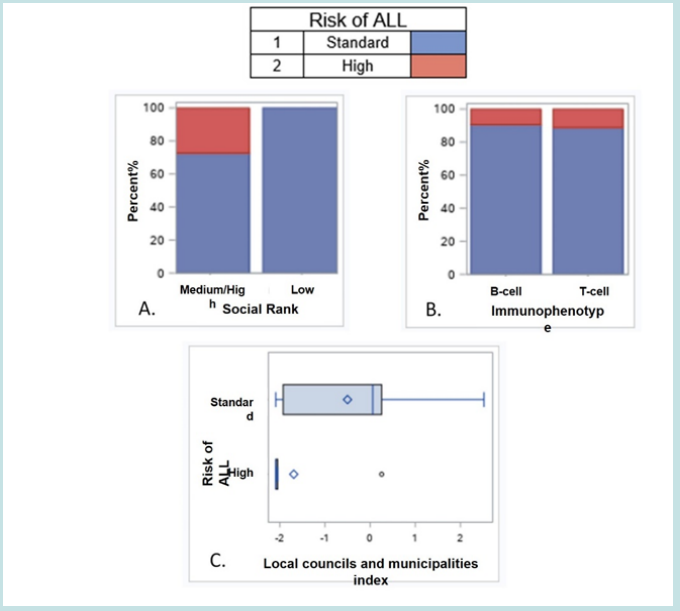

Figure 2: A) Risk of ALL shown according to Social Rank supbroups: Low vs. Medium/high. **B)** Risk of ALL shown according to immunophenotype supbroups: B-cell vs. T-cell. **C)** Risk of ALL shown according to Local councils index subgroups: Standard vs. High.

Ability to Achieve Complete Remission

Second, we wanted to see if patients' ability to achieve complete remission is affected by these demographic characteristics. According to the Fisher exact test, the ability to achieve complete remission was not related to social rank (n=52, p=0.72), ethnicity (n=52, p=0.34), gender (n=52, p=0.60), BMI (n=52, p=0.43), age (n=52, p=0.43), local councils and municipalities socioeconomic index (n=52, p=0.15), Immunophenotype (n=52, p=0.07s) and lab measurements (Table 2). When examining this question through a bivariate analysis using a logistic regression model, we found no significant connections between the listed independent variables, the patients' social rank, and their ability to achieve complete remission, hinting the minor role social ranks play in ALL disease progression.

Rate of Complications

Fever Episodes

AIEOP-BFM ALL 2009, is the treatment protocol given to the paediatric patients with ALL in this study and was 2 years long. Chemotherapy treatments are known to impact the patients' immune system, causing a variety of treatment-related complications due to harming of the immune system such as fever, neutropenia, and bacteraemia [25]. We hoped to understand whether the rate of these complications is affected by the patients' demographic and clinical characteristics. We found significant correlations between social rank and the number of fever episodes (p<0.001), where high social rank patients experienced an average of 9.45 episodes (+/- 6.16), compared to medium/low social rank patients with an average of 6.29 (+/- 4.62), shown in figure 3. Interestingly, a significant correlation between ethnicity and number of fever episodes was not found. Additionally, higher Local councils and municipality index had a weak significant negative correlation with a higher number of fever episodes (p<0.001). This correlation diminished when the variable was run as dichotomic (below and above 0, P=0.07). Age correlated significantly with number of fever episodes as well (p=0.017), with males demonstrating a higher average of episodes 8.35 (+/- 5.23) compared to females 6.55 (+/- 5.8). Immunophenotype correlated with number of fever episodes too, with B cell having an average of 8.14 (+/- 5.8) episodes compared to T-cell with 5.67 (+/- 3.12). Furthermore, BMI, age, CNS status, Haemoglobin, Neutrophils, WBC, Albumin, and CRP correlated significantly with the number of fever episodes, as seen in table 3, though only age and haemoglobin had higher correlation coefficients indicating a strong correlation.

Table 2: The ability to achieve complete remission isn't correlated to any of the tested parameters.

	N	Failed to achieve complete remission		P value
		No	Yes	
Social Rank				
Low n(%)	22(41.5%)	6(33.3%)	12(66.7%)	0.7243
Medium/High n(%)	30(58.5%)	8(29.6%)	19(70.4%)	
Ethnicity				
Jewish n(%)	26(50.0%)	6(25.0%)	18(75.0%)	0.3466
Bedouin n(%)	26(50.0%)	7(35.0%)	13(65.0%)	
Gender				
Male n(%)	30(58.5%)	8(30.8%)	18(69.2%)	0.6029
Female n(%)	22(41.5%)	6(31.6%)	13(68.4%)	
BMI	52	-	-	0.4376
Age (days)	52	-	-	0.4376
Local Councils and Municipalities Socioeconomic index	52	-	-	0.1534
Immunophenotype				
B cell n(%)	42 (81.1%)	9(24.3%)	28(75.7%)	0.0734
T cell n(%)	9(17.0%)	4(57.1%)	3(42.9%)	
B+T cell n(%)	1(1.9%)	1(100.0%)	0(0.0%)	
Hemoglobin	52	-	-	0.234
Neutrophils	52	-	-	0.2499
WBC	52	-	-	0.9722
Albumin	52	-	-	0.2127
CRP	52	-	-	0.97

The Fishers Exact Test was used to determine the relation between the categorial independent variables and the dichotomous outcome variable (failed to achieve complete remission). The relation between the continuous variables and the dichotomous outcome variable (failed to achieve complete remission) was examined using the logistic regression

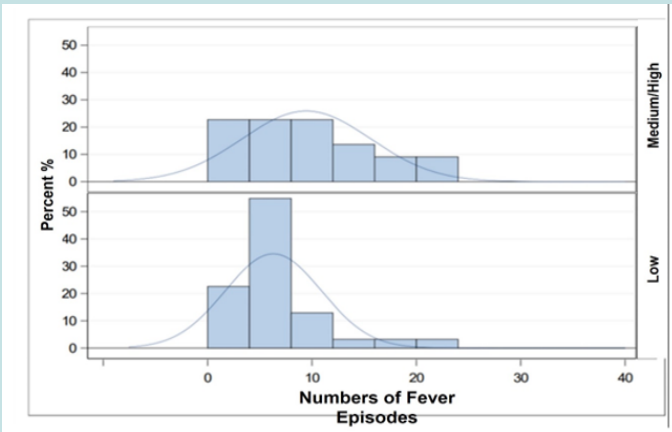

Figure 3: Number of fever episodes is significantly higher in Medium/High social rank patients.

Table 3: The number of fever episodes is significantly correlated to most tested parameters.

	N	Number of fever episodes	P value
Social Rank			
High: Mean ± SD	22	9.45+/-6.16	<0.001
Medium/low: Mean ± SD	30	6.29+/-4.62	
Ethnicity			
Jewish: Mean ± SD	26	7.92+/-5.47	0.5828
Bedouin: Mean ± SD	26	7.50+/-5.60	
Gender			
Male: Mean ± SD	30	8.35+/-5.23	0.0177
Female: Mean ± SD	22	6.55+/-5.80	
BMI			
Pearson's correlation coefficient	52	0.08	<0.001
Age (days)			
Pearson's correlation coefficient	52	-0.31	<0.001
Local Counsils and Municipalities Socioeconomic index			
Pearson's correlation coefficient	52	-0.16	<0.001
Immunophenotype			
B cell: Mean ± SD	43	8.14+/-5.80	0.0115
T cell: Mean ± SD	9	5.67+/-3.12	
CNS Status			
Pearson's correlation coefficient	52	0	<0.001
Hemoglobin			
Pearson's correlation coefficient	52	-0.24	<0.001
Neutrophils			
Pearson's correlation coefficient	52	0.08	<0.001
WBC			
Pearson's correlation coefficient	52	0.04	<0.001
Albumin			
Pearson's correlation coefficient	52	-0.05	<0.001
CRP			
Pearson's correlation coefficient	52	0.02	<0.001

Pearson correlation was used to determine the relation between the categorial independent variables and the dichotomous outcome variable (number of fever episodes).

Episodes of Fever with Neutropenia

When examining correlations between the number of fever episodes accompanied with neutropenia and the patients' social rank, we found a non-significant correlation (p=0.2213). Moreover, the number of fever episodes accompanied with neutropenia correlated significantly only with the patients' neutrophils levels (p=0.027), where lower neutrophil levels indicated a mean of 3.26+/- 2.07 fever episodes accompanied with neutrophilia among all patients.

Episodes of Fever with Neutropenia and Bacteraemia

While analysing associations of the researched parameters with the number of fever episodes accompanied by neutropenia and bacteraemia, a non-significant correlation was found with patients' social rank (p=0.9342), but a significant correlation was found with CRP (p=0.0473), where higher levels of CRP (38+) indicated 0.56+/-1.01 episodes of fever accompanied by neutropenia and bacteremia among all patients.

Discussion

In the following study, we analyzed in retrospect datasets of 52 ALL pediatric patients treated in the hospital of the south of Israel (Soroka). We hoped to understand the impact of social ranks and ethnicities in the south of Israel on the quantity of complications and hospitalizations during the progression of ALL.

First, we aimed to determine whether patients' beginning risk of ALL is impacted by a variety of demographic and clinical parameters of patients during their initial admission to the hospital. A significant relation between higher social ranks and a higher risk of ALL was found, where 27% of Medium/High social ranked patients were considered high risk of ALL, and 100% of low social rank were considered standard risk of ALL. Nevertheless, a significant relation between the risk of ALL and the local councils and municipalities socioeconomic index of patients was found, with higher index associating with higher risk of ALL. Meaning, paediatric patients from higher socioeconomic communities are associated with higher risk of ALL. A previous large study [26] which investigated the incidence of childhood ALL in over 8,000 patients among different socioeconomic positions in the united states found that the incidence rate of childhood ALL was negatively associated with socioeconomic position among Hispanics but was positively associated among children of other races/ethnicities such as- for non-Hispanic whites, non-Hispanic blacks, Asians/Pacific Islanders and American Indians/Alaska Natives. Notably, there is no previous study that examined the specific risk of ALL among the Bedouin and Jewish populations in Israel. It is therefore apparent that there is no clear pattern and correlation between socioeconomic stand and the risk of ALL, and that results very among different populations from the world and different treatment centers. Particularly, our study was done on a small group of patients only from the south of Israel, and not from a large variety of hometowns, which may explain the results and may indicate that conclusions from this data should be made carefully.

Furthermore 100% of patients with a B+T cell Immunophenotype were found with a higher risk of ALL. This finding correlates with what's known in literature regarding this special population of blasts that have a higher incidence of chromosome abnormalities [27], and a higher risk of ALL. Also, as anticipated and previously described, higher levels of WBC at admission are predictive of a higher risk of ALL and a poorer prognosis [28].

We aimed to find whether the same demographic criteria impact patients' outcomes. We found that the ability to achieve complete remission was not related to social rank, ethnicity, gender, BMI, age, local councils and municipalities socioeconomic index, Immunophenotype and lab measurements. These results contrast with literature from different cultures around the world, in which a variety of studies demonstrate different outcomes according to different socioeconomic backgrounds: a study on patients from Florida and Texas demonstrated that patients residing in neighbourhoods with the highest poverty rate had a 1.8-fold increase in mortality compared with patients residing in neighbourhoods with the lowest poverty rate [29]. Another study from Pakistan showed that the overall survival of patients was related to socioeconomic status [4]. This discrepancy may be best explained by the mandatory Israeli healthcare system and the equal medical care patients are given in the south of Israel, which does not change in relation to their socioeconomic background. In contrast, in other countries medical care and treatment may vary according to the parents' ability to pay. A past study found that the degree of pro-rich inequity in doctor use is highest in the United States and Mexico, when compared to other countries, which may explain the impact of socioeconomic positions on ALL survival due to lack of access to equal healthcare among poorer populations [30].

Third, ALL and its chemotherapy treatment are often accompanied by complications in the shape of fever episodes, therefore we aimed to shed light on the likelihood of treatment complications among our ALL paediatric patients according to their social rank. We found a significant correlation between patients' quantity of fever episodes and their social rank, indicating that higher social ranks are associated with more fever episodes (9.45 +/- 6.16). Nevertheless, this significant correlation remains also when data is adjusted to sex and gender. Data regarding the difference in outcomes of ALL patients according to social ranks is vastly described in literature [4,18,20], mostly emphasizing that lower social ranks are associated with worst disease outcomes. However, the frequency of chemotherapy treatment complications among ALL patients specifically, isn't described in literature, highlighting the importance of our findings. Interestingly, a recent study investigated Danish children treated with chemotherapy and demonstrated that inferior physician compliance to protocol recommendations on drug dosage, rather than families' adherence to therapy, may contribute to the association between socioeconomic position and cure rates in childhood ALL [31]. Meaning, patients from lower socio-economic ranks do not receive the full aggressive treatment, leading to less suppression of their immune system and possibly less treatment side effects. Another main possible explanation for our results is as described before, the mandatory Israeli healthcare system and the equal medical care patients are given in the south of Israel. These equal health care conditions probably blur and rule out the impact of socioeconomic positions on the progress of patients' disease, as they create a setting where everybody is treated by the same doctors, facilities, and treatment protocols. Furthermore, parents from lower socioeconomic positions are economically aided when their child is diagnosed with ALL, therefore furthering the closure of the apparent gap in the quality of life of their children.

Finally, the number of fever episodes accompanied with neutropenia correlated significantly only with the patients' neutrophils levels, meaning, as anticipated lower neutrophil levels correlated with more episodes of fever with neutropenia. Additionally, the number of fever episodes accompanied by neutropenia and bacteraemia, correlated significantly only with higher levels of CRP. Both findings, and the fact that both tested complications did not correlate with any other tested parameters, highlights the non-existing correlation between socio-economic position and the rate of complications in the treatment of ALL in paediatric patients. That is, when the tested patients are in an ideal medical environment, where their parents' income and ethnicity does not influence the quality and type of healthcare they're given. Our results suggest that further implementing equal health care to all patients may drastically change the current outcomes and complications rates among different social ranks and ethnicities all over the world.

Our research's limitations are due to its' size, and our criteria of investigation. Firstly, our focus is on a relatively small group of children diagnosed and treated with ALL, whom are from a specific hospital, therefore conclusions from this specific data do not necessarily apply widely. Second, it is hard to compare socioeconomic impacts on patients since it is a very subjective variable which does not have a precise definition and therefore may be defined differently. Third, in Israel, the socioeconomic status changes immediately upon diagnosis- due to government interference- those in a lower economic status might get big financial support which will change their quality of life and even surpass those who are considered middle-class.

To conclude, our results demonstrate several key findings: first, the risk of ALL was higher among the higher class of social economic rank in the south of Israel. Second, the ability to achieve complete remission among pediatric patients with ALL in the hospital of the south of Israel (Soroka) was not impacted by ethnicity and social rank. Third, the number of fever episodes was higher among the higher social rank subgroup of patients, while the number of fever episodes accompanied by neutropenia and bacteremia did not vary, highlighting the non-existing impact of social economic positions on patient's complications rate when in an ideal and pro-equal health care environment.

Conflict of Interest Statement

The authors signed on this manuscript certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Ethical Statement

Ethical Approval was obtained from Institutional Review Board for this study (attached in Hebrew), We'd thank editorial office of "Cancer Reports" for updating this in the system.

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