Universal Journal of Public Health 12(5): 968-980, 2024
DOI: 10.13189/ujph.2024.120520 http://www.hrpub.org

Caregiver Stress and Health Status Based on Self-report Measures, Cortisol Level, and Immune Functioning among Parents of Children with Neurodevelopmental Disorders

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Received June 21, 2024; Revised August 7, 2024; Accepted September 13, 2024

Cite This Paper in the Following Citation Styles

(a): *[1] Krishna Priya Balachandran, Mohanraj Bhuvaneswari , "Caregiver Stress and Health Status Based on Self-report Measures, Cortisol Level, and Immune Functioning among Parents of Children with Neurodevelopmental Disorders," Universal Journal of Public Health, Vol. 12, No. 5, pp. 968 - 980, 2024. DOI: 10.13189/ujph.2024.120520.*

(b): *Krishna Priya Balachandran, Mohanraj Bhuvaneswari (2024). Caregiver Stress and Health Status Based on Self-report Measures, Cortisol Level, and Immune Functioning among Parents of Children with Neurodevelopmental Disorders. Universal Journal of Public Health, 12(5), 968 - 980. DOI: 10.13189/ujph.2024.120520.*

Abstract **Background:** Evaluation and integration of family carers' health concerns into the treatment protocol are imperative. Caregivers of children diagnosed with neurodevelopmental disorders (NDDs) are often involved in extended periods of caregiving resulting in physical and mental exhaustion. The current study aims to examine the stress and health status of parents who are primary carers providing care for children with NDDs by evaluating the caregivers' experience of stress and immune functioning through self-report and biomarker measures. **Methods:** The study was conducted in two phases. The first phase involved the administration of self-report measures of caregiver stress and perceived immune status using the Kingston Caregiver Stress Scale and Immune Status Questionnaire respectively to 150 parents of children with NDDs. In the second phase, 30 parents who fulfilled the criteria and consented to participate in the blood testing were evaluated for biomarker profiles of stress and immune functioning through the cortisol, lymphocytes, and hemoglobin measures. **Results:** The results of the study revealed that of 150 parents 142 (94.6%) experienced moderate-severe stress and 70 (46.6%) perceived reduced or poor immune status. There exists a significant negative relationship between self-reported measures of caregiver stress and perceived immune status and there also exists a significant relationship between self-reported measures and biomarker measures. **Conclusion:** Caregivers of children with NDDs are constrained to navigate through the process of caregiving for an extended duration of their lives which could potentially result in compromised psychological and immune functioning in the long run. Therefore, it is vital to focus on care arrangements for family carers by centering a biopsychosocial model of care for caregivers to improve their well-being.

Keywords Caregiver Stress, Perceived Immune Status, Health, Biopsychosocial, Caregivers, Parents, Neurodevelopmental Disorders, Biomarkers, Cortisol, Lymphocytes, Hemoglobin

1. Introduction

A child diagnosed with a disability can lead to life-altering experiences for parents and can result in an adverse impact on the caregiver's health, functioning, and well-being [1,2]. Parents experience complex parenting or caregiving challenges while providing care for children with neurodevelopmental disorders combined with

behavioral and physical co-morbidities [3]. Neurodevelopmental disorders (NDDs) are a group of conditions that are associated with deficits in domains such as social, cognitive, language, and motor functioning [4].

Caregivers of children with severe neurodevelopmental conditions and co-morbidities exhibited reduced health-related quality of life in comparison with other caregivers [5]. Parents of children with NDDs displayed elevated levels of stress, anxiety, and depression associated with increased caregiver burden [6,7]. In addition to experiencing psychological difficulties, they also experience poorer quality of life, social marginalization, financial difficulties, work-related issues or unemployment, and other caregiving-related challenges based on their life circumstances that could impact their overall well-being [8,9]. These findings have been comprehensively explored and established in research studies related to caregivers of children with NDDs.

Furthermore, research findings indicate that parents of children with NDDs not only experience psychosocial distress but also prominent physical health issues. Parents of children with autism experience sleep deprivation and sleep disturbances that result in serious health problems [10]. Mothers of children with NDDs were more likely to be diagnosed with chronic conditions and possessed higher healthcare service utilization with increased physician visits and intake of prescribed drugs [11]. Similarly, parents of children with developmental disabilities who suffered from depression were associated with negative health outcomes and family outcomes [12]. Rigorous physical demands of providing care for children with cerebral palsy caused amplified volume of back pain and mothers of children with ASD and ID were twice more likely to exhibit risk of death due to cancer, cardiovascular disease, and death by misadventure [13,14,15].

The term ‘biopsychosocial model’ proposed by Engel [16] in 1960 has been widely discussed and researched at present after Engel claimed the ‘biomedical model’ has a reductionistic framework to understand disease or illnesses and outline the limitations of the biomedical approach [17]. Engel broadened the scope of the biomedical model to the biopsychosocial model to include psychosocial factors contributing to illnesses [18]. The biopsychosocial model exemplifies that physical factors such as genes, nutrition, sleep, exercise, and physical activity; psychological factors such as beliefs, coping and emotional states; and social factors such as work, family, relationships, and financial forces largely determine the symptoms, pain, and disability encapsulating the disease or illness among an individual [19].

The foundation for future physicians and medical education has begun to focus on integrating knowledge from behavioral and social sciences into medical practice to enhance psychosocial competence among medical professionals [20]. Certain areas of study such as internal medicine, orthopedics, obstetrics, and gynecology attempt to integrate a biopsychosocial approach paving the way for effective evaluation and treatment [17]. Despite the identification of the caregiver burden through a biopsychosocial approach, the integration of the approach in the evaluation and management of caregiving-related concerns experienced by the carers, especially caregivers of children with neurodevelopmental disabilities, is uncertain [21]. Although several research findings have ascertained parents of children with NDDs experience complex physical and psychosocial distress, health assessments, policies, and practices primarily serve the recognized child with disabilities and not the carers [22], especially in countries like India where informal caregiving is not formally recognized [23].

Caregiving for children with NDDs is a long-term process resulting in chronic stress among caregivers. Chronic stress implies harmful effects on bodily functions [24]. Prolonged stress such as exposure to endured caregiving results in the secretion of bodily chemicals, indicating changes in the body system [25]. The various systems in the body such as the hypothalamic-pituitary-adrenal axis (HPA-axis), autonomic nervous system (ANS), and immune system respond to stressors by secretion of a hormone called cortisol, a significant biomarker of stress [26]. Cortisol is the most common biomarker utilized to compare the physiological stress observed between individuals [27]. Cortisol is a hormonal marker of stress that has received attention across various research studies related to psychological and physical health [28]. Cortisol plays an active role in protein synthesis, regulation of glucose, immune functions, and psychological activity [29]. Cortisol activates the HPA axis while responding to psychosocial stress and interacts with the ANS and immune system [26]. Stress and the immune system interact with each other determining the association between stress and the development of diseases [30].

Limited research studies across the globe have attempted to evaluate the caregiver's stress and immune functioning associated with caregiving for children with NDDs by investigating the biological markers of stress and immune functioning. A few studies of mothers of children with autism noted maternal cortisol dysregulation and a flattened maternal diurnal cortisol profile associated with significant sleep problems [28,31]. Caregivers of children with autism reported health complaints and fatigue associated with their cortisol and immunoglobin A levels [32].

Data collection and analysis regarding self-report measures of perceived immune status and stress and biomarkers, i.e., cortisol, lymphocytes, and hemoglobin, can provide evidence-based information regarding psychophysiological changes and guide policy, care planning, and interventions. This study investigated caregiver stress and immune function based on self-report measures and biomarker profiles, including cortisol, lymphocytes, and hemoglobin of parents of children with NDDs. The current study is an attempt to inform healthcare providers and the general audience of the significance of

testing these biomarkers among carers in regular clinical practice and provide effective treatment and psychosocial interventions for carers as they comprise a notable section of the community.

Objective

1. To assess and examine the relationship between the self-report measure of caregiver stress and perceived immune status among parents providing primary care for children with NDDs.
2. To evaluate stress and immune functioning through biomarker measures such as cortisol hormone - an indicator of stress, lymphocytes- a component of the white blood cells as an indicator of immune function, and hemoglobin- a component of red blood cells that mediates immune response.
3. To examine the relationship between self-report measures and biomarker measures.

Hypotheses

H_{a1}: There exists a significant difference between the level of self-reported caregiver stress and demographic profiles of caregivers such as gender, age, hours spent providing care, occupation, and primary diagnosis of the child.

H_{a2}: There exists a significant difference between the level of self-reported perceived immune status and demographic profiles such as gender, age, hours spent providing care, occupation, and primary diagnosis of the child.

H_{a3}: There exists a significant relationship between the self-report measures of caregiver stress and perceived immune status.

H_{a4}: There exists a significant relationship between self-report measures of caregiver stress, perceived immune status, and biomarker measures (cortisol, lymphocytes, and hemoglobin).

2. Materials and Methods

2.1. Research Design

A quantitative research design was adopted to understand the presence, differences, and relationship between self-reported measures of caregiver stress and perceived immune status and biological measures such as cortisol, lymphocytes, and hemoglobin among carers of children with NDDs.

2.2. Participants

The research was conducted in two phases. A total of 150 parents either mother (n=99) or father (n=51) belonging to the age group of less than or equal to 40 years (n=54) or above 40 years (n=96) involved in the primary care of a child with NDDs were recruited through purposive sampling. The parents resided in the urban areas of Chennai city, Tamil Nadu, India. Few parents also reported migrating from semi-urban and rural areas to access treatment for their children. Parents were either unemployed (n=42), worked for daily wages (n=13), or worked in the government (n=14) and private sector (n=81). The NDDs related to the nervous system that are listed by the Right to Person with Disability (RPwD) Act, 2016, and those that were also found as the common NDDs through a pooled estimate in India were selected for the study [33,34]. Thus, parents caring for children primarily diagnosed with NDDs that include autism spectrum disorder (ASD), intellectual disability (ID), learning disability (LD), and cerebral palsy (CP) along with its associated co-morbidities such as speech and language disability, attention deficit hyperactivity disorder (ADHD) and neurological conditions such as epilepsy and seizures were recruited. Inclusion criteria included parents between the age group of 25-55 providing care for at least two years or more for a child aged between 5-17 years, diagnosed with ASD, ID, LD, and CP and its associated co-morbidities.

Exclusion criteria included parents caring for children with other NDDs apart from the ones selected for the current study or other chronic illnesses or caring for another significant person diagnosed with any chronic condition within the family. In the second phase, 30 parents who scored ‘severe’ on caregiver stress and ‘poor’ or ‘reduced immune status’ on perceived immune status measures, fulfilling the inclusion criteria, and those who voluntarily consented were tested for the biomarkers through a blood test. Parents diagnosed with any chronic psychiatric problem or health conditions such as diabetes, thyroid, asthma, or hypertension and who are actively on medication were not included in the blood testing.

2.3. Procedure

All parents were recruited from three established non-profit special schools registered under the government of Tamil Nadu located in the city of Chennai, Tamil Nadu, India. The authorities of the special schools were approached and sought permission. Parents of children with NDDs who consented to participate in the present study were recruited. Written informed consent was obtained from all the parents before initiating the research study. The research was conducted in two phases: The first phase involved the administration of standardized measures called the Kingston Caregiver Stress Scale and Immune Status Questionnaire to assess self-reported caregiver stress and the perceived immune status of the parents respectively. The two questionnaires were administered to 150 parents of children with NDDs related to the nervous system: LD, ID, ASD, and CP and its associated co-morbidities. The questionnaires were administered to parents of children with NDDs in person

through paper-pencil tests within the school premises by the researcher, a qualified counseling psychologist, holding a master's degree in counseling psychology. In the second phase, 30 participants who consented to a blood test to assess the biomarkers (cortisol, lymphocytes, and hemoglobin) were tested for the biomarker profile. The parents were briefed about the procedure and ensured the utmost confidentiality and safety of the invasive method of drawing blood for biomarker testing.

Parents who volunteered for blood tests were asked to report between 7-8 AM, 30 minutes after awakening without consuming any food. A blood test was carried out to test for cortisol hormone and a complete blood count (CBC) test to obtain lymphocyte and hemoglobin profiles by a qualified lab technician who has completed a diploma in medical laboratory technology. The technician drew 4 ml of blood from each participant and was tested in a diagnostic laboratory to assess for the biomarkers. The institutional ethical committee had approved the research study and data collection procedure.

2.4. Measures

2.4.1. Sociodemographic Details

The sociodemographic details of each parent such as age, gender, occupation, relationship with the child, time spent providing care, and child's information such as age, gender, diagnosed neurodevelopmental condition, and other necessary details were obtained before the administration of the questionnaires.

2.4.2. Psychological Measures

Kingston Caregiver Stress Scale (KCSS)

The Kingston Caregiver Stress Scale (KCSS) was developed by Hopkins and Kiliks [35] in 2016 to assess the level of perceived stress reported by a caregiver. The questionnaire is designed for informal or family carers and not for formal institutional care staff. The scale consists of 10 items. KCSS possesses sound reliability scores with internal consistency- Cronbach alpha for complete scale as 0.89, caregiving domain as 0.88, family domain as 0.88. The maximum and minimum scores that can be obtained are 50 and 10 respectively. A score below 16 indicates mild stress, 16-24 indicates moderate stress, and above 24 indicates severe stress.

Immune Status Questionnaire (ISQ)

The Immune Status Questionnaire (ISQ) was developed by Versprille and Colleagues [36] in 2019 to assess the perceived immune status of an individual. The ISQ consists of 7 items and aims to assess perceived immune status over the past month. Predictive validity of 85% and convergent validity established by significant correlation with 1 item perceived immune functioning ($r=0.383$, $p<0.0001$) and test-retest reliability of ($r=0.80$). The maximum and minimum scores obtained are 28 and 0 respectively. A higher raw score indicates compromised immune functioning. The raw score is converted as a final score to indicate the perceived immune status. 0 indicates poor immune functioning, 10 indicates excellent perceived immune functioning and less than 6 indicates reduced immune functioning.

2.4.3. Biological Measures

Biological measures (cortisol, lymphocytes, and hemoglobin) were assessed to measure the stress and immune functioning respectively among the parents.

Cortisol

The neuroendocrine-stress response system produces and secretes hormones into the bloodstream from the hypothalamus, pituitary, and adrenal glands [37]. The cortisol test measures the amount of cortisol, a hormone secreted by the adrenal cortex that is present in the circulatory system at a given point in time. Cortisol level often fluctuates during the day. The highest levels of cortisol are at around 6-8 AM and the lowest levels are during the night. The normal reference range for cortisol (tested at AM) is 3.7-19.4 ug/dl (microgram per decilitre).

Lymphocytes

White blood cells (WBC) are an important component of the immune system that protects and fights against infections in the body. The WBC adult reference value ranges from 4000-11000 cells per cubic millimeter (cumm). In the current investigation lymphocyte, a component of WBC, an indicator of immune function, that helps an individual's body's immune system fight against foreign viruses and bacteria was measured. The lymphocyte reference range is between 30-50% of total WBC. Therefore, the normal absolute lymphocyte count ranges between 3300-5500 cells/cumm of the total WBC count.

Hemoglobin

Hemoglobin is a vital component of red blood cells (RBC) responsible for carrying oxygenated blood from the lungs to tissues and transporting carbon dioxide blood back to the lungs. Although the primary function of hemoglobin is oxygen carriage, it also participates in the mediation of immune response [38]. Therefore, in addition to lymphocytes, hemoglobin measure was also taken into consideration. The reference range for hemoglobin in men ranges between 13.5-17 grams per decilitre (gms/dl) and for females it ranges between 12-15.3 gms/dl.

It is important to note that the normal reference range for each of these biomarkers may vary slightly among different laboratories.

2.5. Data Analysis

The obtained data were analyzed using the Statistical Package for the Social Sciences (SPSS), IBM® SPSS® Statistics version 23.0. The data was analyzed through

descriptive statistics such as percentage, mean, and standard deviation and inferential statistics such as Pearson's product-moment correlation to examine the relationship between the self-reported and biomarker measures, independent sample t-test, analysis of variance, and post-hoc analysis to determine the differences in the measures among distinct demographic groups.

3. Results

3.1. Demographic Information

From Table 1, it can be inferred that the majority of the participants were mothers (n=99) of children with NDDs such as CP (n=40), autism (n=40), ID (n=38), and LD (n=32) who took part in the phase 1 survey study as primary caregivers. The participants belonged to an age group between 25 and 55 and most of them were working in the private sector (n=81) and provided care for 4-8 hours (n=62) or 9-16 hours (n=54), for more than 5 years (n=120). From phase one of the study, it was identified that of 150 parents, 142 (94.6%) experienced moderate-severe stress and 70 (46.6%) perceived reduced or poor immune status. In phase 2 of the study, 30 caregivers consented to blood testing of which 18 were female and 12 were male providing care for children with CP (n=10), autism (n=10), and ID (n=10) belonging to an age group of 22-55 years, either unemployed (n=6) or employed in daily wage (n=4), private (n=18) or government (n=2) sector and spent varied time providing care.

Table 1. Demographic information of parents participating in phase-1 (survey) and phase-2 (blood-testing) of the study

Demographics		Phase 1 (N=150)	%	Phase 2 (N=30)	%
	≤ 40	54	36	18	60
Age	> 40	96	64	12	40
	Female	99	66	18	60
Gender	Male	51	34	12	40
	Government	14	9.33	2	6.7
	Private	81	54	18	60
	Unemployed	42	28	6	20
Occupation	Daily wage	13	8.67	4	13.3
	Mother	99	66	18	60
Relationship with child	Father	51	34	12	40
	Less than 4 hours	22	14.67	-	-
	4-8 hours	62	41.33	12	40
	9-16 hours	54	36	12	40
Hours Spent Providing care	More than 16 hours	12	8	6	20
	Less than 2 years	-	-	-	-
	2-5 years	30	20	8	26.7
Number of years providing care	More than 5 years	120	80	22	73.3
	Autism	40	26.67	10	33.3
	Cerebral Palsy	40	26.67	10	33.3
	Intellectual disability	38	25.33	10	33.4
Primary diagnosis of the child	Learning disability	32	21.33	-	-

3.2. Independent Sample t-test

An Independent sample t-test was conducted to compare the level of self-reported caregiver stress among caregivers of distinct gender and age groups. From Table 2, it can be inferred that there exists no significant difference in the level of caregiver stress concerning males (M=27.86, SD=8.90) and females (M=28.94, SD=6.70); t (148) = .831, p=.407, d=0.14. Similarly, no significant difference exists between caregiver stress concerning carers less than or equal to 40 years of age (M=28.96, SD=6.84) and above 40 years (28.35, SD=7.88); t (148) =-.475, p=.635, d=-0.08. This indicates that caregiver stress is present to the same extent among caregivers belonging to both genders of parents (mother and father) and diverse age groups, providing care for their children with NDDs.

Likewise, an independent sample t-test was conducted to compare the level of self-reported perceived immune status. There exists no significant difference between perceived immune status among caregivers of distinct genders and age groups. From Table 3, it can be inferred that there exists no significant difference in the level of perceived immune status between males (M=6.90, SD=2.29) and females (M=6.22, SD=2.62); t(148)=-1.570, p=.119, d=-0.27, and among carers who are less than or equal to 40 (M=6.28, SD=2.59) and above 40 years of age (M=6.55, SD=2.49); t(148)=.638, p=.525, d=0.11. This indicates that caregivers of both genders and across age groups perceived having similar immune status.

3.3. Analysis of Variance

One-way Analysis of Variance (ANOVA) was carried out to understand the difference in the level of self-reported caregiver stress and perceived immune status with hours spent providing care, occupation, and primary diagnosis of the child (Table 4). The study reveals that there exists no significant difference in the level of caregiver stress and perceived immune status among varied hours spent providing care or distinct occupations. However, a significant difference existed in the levels of both self-reported caregiver stress [F (3,146) = 43.118, p = 0.000] and perceived immune status [F (3,146) = 10.370, p = 0.000] based on the primary diagnosis of the child for which the caregiver is providing care.

The post hoc test further conducted using Tukey HSD reveals a significant difference ($p<0.05$) in the caregiver stress between carers of children with LD (M=19.00, SD=4.670), and ASD (M=29.98, SD=6.727), LD (M=19.00, SD=4.670) and CP (M=33.05, SD =5.840), and LD (M=19.00, SD=4.670) and ID (M=30.45, SD=4.298). Hence, we can conclude that the stress levels experienced by caregivers of children with NDDs are different. Based on the mean scores, the highest caregiver stress is reported by parents of children with CP followed by ID, ASD, and LD. Similarly, in the case of self-reported perceived immune status, the test reveals a significant difference ($p<0.05$) in the level of perceived immune status between carers of children with ASD (M=7.65, SD=1.916) and CP (M=5.05, SD=2.891), ASD (M=7.65, SD=1.916) and ID (M=5.97, SD=1.852). Likewise, the test reveals a significant difference in the perceived immune status of carers of children with CP (M=5.05, SD=2.891) and LD (M=7.28, SD=2.453). Hence, we can conclude that the level of perceived immune status among carers also differs for different NDDs of children whom they are providing care for. Based on the mean scores, poor or reduced perceived immune status is reported by parents of children with CP followed by ID, ASD, and LD.

Table 2. Independent sample t-test for caregiver stress

Demographic variables	Caregiver Stress						
Gender	Male (n=51)		Female (n=99)				
	M	SD	M	SD	t (148)	p	Cohen's d
	27.86	8.90	28.94	6.70	.831	.407	0.14
Age	≤ 40 (n=54)		>40 (n=96)				
	M	SD	M	SD	t (148)	p	Cohen's d
	28.96	6.84	28.35	7.88	-.475	.635	-0.08

Table 3. Independent sample t-test for perceived immune status

Demographic variables	Perceived Immune Status						
Gender	Male (n=51)		Female (n=99)				
	M	SD	M	SD	t (148)	p	Cohen's d
	6.90	2.29	6.22	2.62	-1.570	.119	-0.27
Age	≤ 40 (n=54)		>40 (n=96)				
	M	SD	M	SD	t (148)	p	Cohen's d
	6.28	2.59	6.55	2.49	.638	.525	0.11

Table 4. Analysis of variance

Variables	Demographic variables	n	M	SD	F	Sig
Caregiver Stress	Hours spent providing care					
	Less than 4 hours	22	27.18	8.157	.530	.662
	4-8 hours	62	28.90	8.323		
	9-16 hours	54	29.09	6.816		
	More than 16 hours	12	27.08	4.522		
	Occupation					
	Government	14	28.86	8.883	.315	.814
	Private	81	28.12	8.027		
	Daily wage	13	28.15	1.743		
	Unemployed	42	29.48	.991		
	Diagnosis of the child					
	Autism	40	29.98	6.727	43.11**	.000
	Cerebral Palsy	40	33.05	5.840		
	Intellectual disability	38	30.45	4.298		
	Learning disability	32	19.00	4.670		
Perceived Immune Status	Hours spent providing care					
	Less than 4 hours	22	6.95	2.478	.364	.779
	4-8 hours	62	6.40	2.695		
	9-16 hours	54	6.37	2.587		
	More than 16 hours	12	6.17	1.193		
	Occupation					
	Government	14	5.57	2.848	.750	.524
	Private	81	6.64	2.277		
	Daily wage	13	6.23	1.423		
	Unemployed	42	6.45	3.086		
	Diagnosis of the child					
	Autism	40	7.65	1.916	10.370**	.000
	Cerebral Palsy	40	5.05	2.891		
	Intellectual disability	38	5.97	1.852		
	Learning disability	32	7.28	2.453		

Note: N=150 parents, ** Significant at 0.01 level

Table 5. Pearson's Product moment correlation for Phase 1 study

Variables	M	SD	Caregiver stress	Perceived immune status
Caregiver stress	28.57	7.509	1	
Perceived immune status	6.45	3.693	-.376**	1

Note: N=150 parents, **p<0.01

Table 6. Pearson's product-moment correlation for Phase 2 study

	Variables	M	SD	1	2	3	4	5
1.	**Lymphocytes**	2889.98	875.7	1				
2.	**Cortisol**	10.78	3.006	.019	1			
3.	**Haemoglobin**	12.11	2.4308	.344	.481**	1		
4.	**Caregiver Stress**	34.30	3.334	.584**	-.134	.367*	1	
5.	**Perceived Immune Status**	4.67	1.516	-.018	-.770**	-.476**	-.082	1

Note: N=30 parents, **p<0.01, *p<0.05

3.4. Pearson's Product Moment Correlation for Phase 1 Study

Pearson's product-moment correlation test was conducted to identify the relationship between self-reported caregiver stress and perceived immune status. From Table 5, it can be observed that there exists a significant negative relationship between caregiver stress and perceived immune status ($r(148) = -.376$, $p<0.01$) among parents of children with NDDs. This indicates that an increase in caregiver stress decreases the caregiver's perception of having a good health status resulting in the perception of having reduced immune status or functioning.

3.5. Pearson's Product Moment Correlation for Phase 2 Study

Pearson's product-moment correlation test was conducted to understand the relationship between the self-report and biomarker measures. From Table 6, it is inferred that there exists a significant positive relationship between lymphocytes and self-reported caregiver stress [$r(28) =.584$, $p< 0.01$], cortisol, and hemoglobin [$r(28)=.481$, $p<0.01$], hemoglobin and self-reported caregiver stress [$r(28)=.367$, $p<0.05$), and a negative relationship between cortisol and perceived immune status [$r(28)=-.770$, $p<0.01$], hemoglobin and perceived immune status [$r(28)= -.476$, $p<0.01$). This indicates that although the correlation coefficient (r) is not strong enough between the biomarkers and self-report measures, it still suggests a significant relationship between the parameters depicting a relationship between the self-reported measures and the biomarker measures indicating there is a potential link between caregivers' stress, health status, and biomarkers associated with stress and immune functioning (cortisol, lymphocytes, and hemoglobin).

4. Discussion

The groundbreaking research on caregivers' health was initiated by Kiecolt-Glaser and colleagues [39] in 1987, revealing that carers of individuals with Alzheimer's exhibited decreased levels of various immune markers compared to non-caregivers. These studies are based on the conceptual narrative that caregiving is a long-term, stressful situation that may have negative consequences on the carers' health [40]. The extended nature and complexities of caregiving for children with NDDs for years could result in caregiver burden pointing out the physical, psychological, financial, and social effects of caregiving [3,10]. The stress and immune status of the primary carers of children with NDDs can predict the long-term functioning of the carers. Thus, it is vital to evaluate the stress and immune status of carers such that, cognizance regarding the caregiver community would enable professionals to adopt an interdisciplinary approach to developing therapeutic and preventative interventions to help the carers.

Findings from the present study reveal a significant relationship between self-reported measures of stress and perceived immune status and biomarker measures of stress and immune functioning (cortisol, lymphocytes, and hemoglobin). These findings suggest a potential link between caregiver stress, immune status, and biomarkers associated with stress and immune functioning in caregivers of children with NDDs. Caregivers are exposed to innumerable acute stress on an everyday basis, and this is linked to disturbances in the hypothalamic-pituitary-adrenal (HPA) axis and the immune system, debilitating the carers' health [41]. From Table 6, it is indicative that the mean absolute lymphocyte count of the caregivers (2889.98 cells/cumm) is observed to be slightly below the normal reference range (3300-5500 cells/cumm) of the total WBC count, suggestive of vulnerability to reduced immune functioning in the long-term if the lymphocyte count continues to go exponentially below or above the normal reference range of lymphocyte count to a greater extent. The finding is congruent with the self-report measures of perceived immune status in which the overall mean score indicates reduced perceived immune status among the carers. While the mean score of cortisol levels was within the reference range, the mean scores of the self-report measure of caregiver stress revealed that carers experienced severe stress during the caregiving process suggesting the presence of extreme stress as a subjective measure in contrast to an objective measure of blood test. The mean score of hemoglobin levels indicates that it's at the lower end of the normal range. This borderline hemoglobin level suggests that if caregivers do not adequately address and adopt necessary measures to

maintain optimum hemoglobin levels, it may potentially predispose to mild anemia and its associated symptoms such as fatigue or weakness over time mimicking reduced or poor immune status [42].

Psychological stress is one of the major factors contributing to reduced immune response against viruses and bacteria [43]. The findings of the current study pave the way to focus on the advancement of caregiver research in the field of psychoneuroimmunology (PNI) describing the interaction between the neuroendocrine and immunological systems and its bidirectional influence on psychophysiological diseases [44]. Thus, this study as an initial step focuses on the interplay of caregiver stress and immune functioning to understand the psychoneuroimmunological aspects of carers. Recent caregiving research has broadened its horizon to focus on stress and immune markers in younger caregiver populations such as parents [45]. Upon analysis of the data, it was identified that there exists a significant negative relationship between self-reported caregiver stress and perceived immune status, through which it can be inferred that caregivers reporting severe stress, perceived poor or reduced immune status which is consistent with the existing findings that reveal that caregiving alters immunity and stress hormones [45]. Therefore, hypothesis (H_{a3}) was accepted.

Similarly, a significant relationship was identified between self-reported caregiver stress and lymphocyte, cortisol and hemoglobin, cortisol and self-reported perceived immune status, hemoglobin and self-reported caregiver stress, and hemoglobin and perceived immune status suggesting a presence of interrelationship between the self-reported measures of caregiver stress, perceived immune status, and biomarker measures among carers of children with NDDs. Therefore, hypothesis (H_{a4}) was accepted. The findings are supported by existing studies on carers that reveal lower concentrations of serum cortisol among carers of cancer patients, dysregulation of hair cortisol in caregivers of dementia patients, and dysregulation of cortisol and immune markers in carers of children with autism [46,47,28,31,32]. Nevertheless, the dearth of such substantial findings for carers of children with NDDs in India to understand the interplay of carers' stress and biomarker measures, limits the scope of drawing generalized inferences but opens doors for further research.

The current study also attempted to evaluate the sociodemographic differences that exist in the self-reported measures of caregiver stress and perceived immune status among the carers of children with NDDs. The findings disclose that there exists no significant difference in the level of caregiver stress and perceived immune status among various demographic profiles of parents of children with NDDs such as age, gender, hours spent providing care, and occupation. However, a significant difference in caregiver stress and perceived immune status was noticed among parents providing care for distinct NDDs. Therefore hypotheses (H_{a1} and H_{a2}) are partially accepted. The findings indicate that a moderate to severe level of stress and reduced to poor perceived immune status were reported by caregivers across diverse demographic characteristics. Although a majority of the existing studies focus on maternal stress, few studies including the present research emphasize parental stress and show similar levels of stress among mothers and fathers of children with ASD and other NDDs [48,49]. A review of caregiving literature establishes that the negative consequences of caregiving on cortisol and immunity are not limited to older caregivers but also among young carers such as young parents providing care, suggesting that stress and immune dysfunction have an apparent effect of caregiving across all age groups [45].

Similarly, all parents regardless of their occupation and hours spent providing care for children with NDDs showed comparable caregiver stress and perceived immune status indicating the complexity of caregiving across all the demographic profiles. However, it was noteworthy to identify that there existed a significant difference in the level of caregiver stress and perceived immune status in parents caring for children with distinct NDDs indicating a substantial difference between learning disability and other NDDs. A study by Craig et al. [4] revealed that parental stress was greater among parents of children with ASD than LD suggesting how the level or severity of physical, emotional, and behavioral problems of children are associated with higher levels of parenting stress. Chronic disabling conditions of children diagnosed with distinct NDDs possessing both medical and mental problems affecting their ADL and executive functioning, create extra demand for parents resulting in stress [50].

Thus, from the current study, it can be deduced that caregiving stress could potentially result in physical strain and have negative effects on the bodily system altering the composition of the circulating biomarkers of the immune system and the endocrine system potentially resulting in compromised immune functioning and elevated levels of stress among carers of children with NDDs. Although results indicate a small but significant relationship between caregiver stress, perceived immune status, and other biomarker measures, further prospective and longitudinal research studies on the lines of caregiving and its associated alteration of immunity must be extensively studied.

The above-described findings of the self-reported caregiver stress and perceived immune status measures along with the immune-endocrine biomarker measures could be attributed to the chronic stress experienced by the parents due to caregiving and its associated roles and responsibilities resulting in stress habituation impacting the psychobiological responses in the long run [32]. Dysregulated endocrine and immune responses of the carers could directly affect the physical and mental health reducing the psychobiological capacity of the caregivers to effectively cope with caregiving stressors and provide care [41]. Exposure to chronic stress among carers could potentially toil the cardiovascular, immune, and

gastrointestinal systems and also result in cognitive impairments [51,52]. Therefore, it is imperative to conduct regular health assessments and focus on developing and implementing psychoneuroimmunology-based interventions focused on cognitive-behavior therapy, mindfulness approach, stress management, and lifestyle modifications [53]. Parents of children with different types of NDDs should be provided with an accessible healthcare system and interventions to improve their biopsychosocial outcomes.

5. Conclusions

By examining the caregiver stress and immune status of the carers through self-report measures and biomarkers, this study established that most carers reported experiencing moderate to severe levels of stress and reduced or poor perceived immune status. In phase 1 of the study, a relationship between self-reported caregiver stress and perceived immune status was confirmed indicating a relationship between elevated stress and reduced perceived immune status. In phase 2 of the study, it was established that there exists a relationship between the self-reported measures and biomarkers of stress and immune functioning. This suggests that there is a potential link between the self-reported measures and the biomarker measures of stress and immune functioning through blood testing indicating the need to direct attention toward the healthcare arrangements for the caregiving community.

6. Implications

The findings of the current study suggest that caregiver stress is often associated with a range of negative consequences, including increased risk of medical conditions, psychological distress, and social challenges over time. Focusing on care arrangements for caregivers by adopting a biopsychosocial model would benefit the carers to seek assistance through the adoption of medico-social strategies to deal with their caregiving challenges effectively. Caregivers of children with NDDs are constrained to navigate through the process of caregiving for an extended duration of their lives resulting in physical and mental exhaustion. Therefore, regular health assessments, medical assistance, recognition of carers' needs through multidisciplinary healthcare professionals, and established social support policies for carers would bring the most out of the caregivers' community enabling them to be empowered by making caregivers' concerns a public health priority.

7. Strength, Limitations, and Future Recommendation

Previous studies focusing on caregiver stress and immunity have centered their attention on caregivers providing care for a specific neurodevelopmental condition, especially autism, or a specific psychiatric or medical condition such as dementia. Conversely, the key focus of the current study was to adopt a non-categorical approach to evaluating caregiver stress and immune functioning among selected NDDs. This could pose potential bias due to heterogeneity in the selected NDDs. The phase 2 (blood testing) study consists of a smaller sample size due to the invasive nature of the investigation and the difficulty in obtaining consent from the carers for blood testing. The blood test assessing biomarkers such as cortisol, lymphocytes, and hemoglobin was carried out only one time and thus, it could have variations based on the time at which the blood was drawn. Future studies could focus on exploring the levels of other endocrine and immunological biomarkers, tested at multiple time intervals among the carers. The cross-sectional design of the study limits causal inferences between caregiver stress, immune status, and biomarkers. Confounding variables such as financial stress, nutritional status, domestic violence, stigma, and other factors that influence caregivers' health are not examined in this study. Future research could carry out mediating and moderating effect analysis to investigate the interplay of multiple factors on caregiver health.

Acknowledgments

The authors would like to extend their heartfelt gratitude to the primary carers of children with neurodevelopmental disorders for taking out time to fill out the questionnaire and cooperating with the blood-testing procedure. The authors would also like to thank the authorities of the educational institute, the special school's management, the lab technician, and the diagnostic laboratory for offering support and resources throughout the investigation.

Statement of Ethics

The research adheres to the International Committee of Medical Journal Editors (ICMJE) guidelines for conducting, reporting, editing, and publication. The current study is a part of the author's doctoral program. The Institutional Ethical Committee for Studies on Human Subjects (IECH) has approved the proposed doctoral study focusing on the biopsychosocial concerns and well-being of the primary caregivers of children with NDDs.

Conflict of Interest

The authors declare no competing interests concerning the research, authorship, and publication of this article.

Authors Contribution Details

The conceptualization, design, literature search, data

collection, data analysis, tabulation, and manuscript preparation were carried out by the first author Krishna Priya Balachandran (KPB), and the corresponding author Mohanraj Bhuvaneswari (MB) was involved in strategizing, data analysis, manuscript editing, manuscript review, and took the responsibility to supervise the integrity of the work.

Funding

The authors received no financial support from any funding agency for the conduction of this research.

Informed Consent

Written consent was taken from all the primary caregivers to participate in the current research. Participants were informed of the anonymity of their identity, the confidentiality of their responses, and the voluntary nature of the study before obtaining consent.

REFERENCES

[1] Ashum G, Singhal N, "Positive perceptions in parents of children with disabilities," Asia Pacific Disability Rehabilitation Journal, vol. 15, no. 1, pp. 22-35, 2004. https://www.researchgate.net/publication/228983336_Positive_perceptions_in_parents_of_children_with_disabilities

[2] Novak-Pavlic M, Rosenbaum P, Macedo LG, Di Rezze, B., Yong, J., Noori, A., & Hughes D, "Effectiveness of Interventions to Promote Physical, Psychological, and Socioeconomic Well-being Outcomes of Parents of Children with Neurodevelopmental Disabilities: Protocol for a Systematic Review," JMIR Research Protocol, vol. 11, no. 7, 2022. DOI: 10.2196/38686

[3] Lach LM, Kohen DE, Garner RE, Brehaut JC, Miller AR, Klassen AF, Rosenbaum PL, "The health and psychosocial functioning of caregivers of children with neurodevelopmental disorders," Disability and Rehabilitation, vol. 31, no. 9, pp. 741–752, 2009. DOI: 10.1080/09638280802242163

[4] Craig F, Operto FF, De Giacomo A, Margari L, Frolli A, Conson M, Ivagnes S, Monaco M, Margari F, "Parenting stress among parents of children with Neurodevelopmental Disorders," Psychiatry Research, vol. 242, pp. 121–129, 2016. DOI: 10.1016/j.psychres.2016.05.016

[5] Trofin CS, Iacob CI, "Health-related quality of life in caregivers of children with and without neurodevelopmental disorders during the COVID-19 pandemic," International Journal of Developmental Disabilities, pp. 1-9, 2023. DOI:10.1080/20473869.2023.2236797

[6] Alsaad AJ, Al Khamees MM, Alkadi AN, Alsaleh MA, Alshairdah AS, Alessa ZA, "Factors associated with the prevalence of depression and anxiety among parents of children with neurodevelopmental disorders in Saudi Arabia," BMC Public Health, vol. 23, no.1, pp. 2320, 2023. DOI: 10.1186/s12889-023-17228-9

[7] Fatima N, Chinnakali P, Rajaa S, Vikas M, Nivedita M, Venkatesh C, "Prevalence of depression and anxiety among mothers of children with neuro-developmental disorders at a tertiary care center, Puducherry," Clinical Epidemiology and Global Health, vol. 11, 2021. DOI: 10.1016/j.cegh.2021.100792.

[8] Faden YS, Merdad N, Faden AY, "Parents of Children With Neurodevelopmental Disorders: A Mixed Methods Approach to Understanding Quality of Life, Stress, and Perceived Social Support," Cureus, vol. 15, no. 4, 2023. DOI: 10.7759/cureus.37356

[9] Tokić A, Slišković A, Nikolić Ivanišević M, "Well-Being of Parents of Children with Disabilities—Does Employment Status Matter?," Social Sciences, vol. 12, no. 8, pp. 463, 2023. DOI: 10.3390/socsci12080463

[10] Bonis S, "Stress and Parents of Children with Autism: A Review of Literature," Issues in Mental Health Nursing, vol. 37, no. 3, pp. 153-163, 2016. DOI: 10.3109/01612840.2015.1116030

[11] Arim RG, Miller AR, Kohen DE, Gu èvremont A, Lach LM, Brehaut JC, "Changes in the health of mothers of children with neurodevelopmental disabilities: An administrative data study," Research in Developmental Disabilities, vol. 86, pp. 76-86, 2019. DOI: 10.1016/j.ridd.2018.12.007

[12] Gallagher S, Hannigan A, "Depression and chronic health conditions in parents of children with and without developmental disabilities The growing up in Ireland cohort study," Research in Developmental Disabilities, vol. 35, no. 2, pp. 448-454, 2014. DOI: 10.1016/j.ridd.2013.11.029.

[13] Tonga E, Düger T, "Factors affecting low back pain in mothers who have disabled children," Journal of Back and Musculoskeletal Rehabilitation, vol. 21, no. 4, pp. 219-226, 2008. DOI: 10.3233/BMR-2008-21401

[14] Tong HC, Haig AJ, Nelson VS, Yamakawa KS, Kandala G, Shin KY, "Low Back Pain in Adult Female Caregivers of Children With Physical Disabilities," Archives of Pediatrics and Adolescent Medicine, vol. 154, no. 11, pp. 1128-1133, 2003. DOI: 10.1001/archpedi.157.11.1128

[15] Fairthorne J, Hammond G, Bourke J, Jacoby P, Leonard H, "Early Mortality and Primary Causes of Death in Mothers of Children with Intellectual Disability or Autism Spectrum Disorder: A Retrospective Cohort Study," PLoS One, vol. 9, no. 12, 2014. DOI: 10.1371/journal.pone.0113430

[16] Engel GL, "A unified concept of health and disease," Perspectives in Biology and Medicines, vol. 3, pp. 459-485, 1960. DOI: 10.1353/pbm.1960.0020

[17] Farre A, Rapley T, "The New Old (and Old New) Medical Model: Four Decades Navigating the Biomedical and Psychosocial Understandings of Health and Illness," Healthcare (Basel), vol. 5, no. 4, pp. 88, 2017. DOI: 10.3390/healthcare5040088

[18] Engel GL, "The clinical application of the biopsychosocial model," The American Journal of Psychiatry, vol. 137, no. 5, pp. 535-544, 1980. DOI: 10.1176/ajp.137.5.535

[19] Roberts A. "The biopsychosocial model: Its use and abuse," Medicine Health Care and Philosophy, vol. 26, no. 3, pp.

367-384, 2023. DOI: 10.1007/s11019-023-10150-2

[20] Frenk J, Chen L, Bhutta ZA, Cohen J, Crisp N, Evans T, Fineberg H, Garcia P, Ke Y, Kelley P, Kistnasamy B, Meleis A, Naylor D, Pablos-Mendez A, Reddy S, Scrimshaw S, Sepulveda J, Serwadda D, Zurayk H, "Health professionals for a new century: transforming education to strengthen health systems in an interdependent world," Lancet, vol. 376, no. 9756, pp. 1923-1958, 2010. DOI: 10.1016/S0140-6736(10)61854-5

[21] Wilson CF, Turnbull S, Gadon L, "Connecting, learning, supporting: Caregivers' experiences of a stress and distress biopsychosocial group intervention," Dementia (London), vol. 23, no. 1, pp. 23-40, 2024. DOI: 10.1177/14713012231207946.

[22] Dykens EM, Fisher MH, Taylor JL, Lambert W, Miodrag N, "Reducing Distress in Mothers of Children with Autism and Other Disabilities: A Randomized Trial," Pediatrics, vol. 134, no. 2, pp. 454-63, 2014. DOI: 10.1542/peds.2013-3164

[23] K. S. Shaji, M. S. Reddy, "Caregiving: A Public Health Priority," Indian Journal of Psychological Medicine, vol. 34, no. 4, pp. 303-305, 2012. DOI: 10.4103/0253-7176.108191

[24] Schneiderman N, Ironson G, Siegel SD. "Stress and Health: Psychological, Behavioral, and Biological Determinants," Annual Review of Clinical Psychology, vol. 1, no. 1, pp. 607-628, 2005. DOI: 10.1146/annurev.clinpsy.1.102803.144141

[25] Mountcastle L, Zajdel M, Robinson T, Keller KR, Gelles S, Livinski AA, Kikani B, Lea DE, Koehly LM, "The Impact of Caregiving for Children with Chronic Conditions on the HPA Axis: A Scoping Review," Frontiers in Neuroendocrinology, vol. 69, 2023. DOI: 10.1016/j.yfrne.2023.101062

[26] Nater UM, Skoluda N, Strahler J, "Biomarkers of stress in behavioural medicine," Current Opinion in Psychiatry, vol. 26, no. 5, pp. 440-445, 2013. DOI: 10.1097/YCO.0b013e328363b4ed

[27] Nepomnaschy PA, Lee TCK, Zeng L, Dean CB, "Who is stressed? Comparing cortisol levels between individuals," American Journal of Human Biology, vol. 24, no. 4, pp. 515-525, 2012. DOI: 10.1002/ajhb.22259

[28] Seltzer MM, Greenberg JS, Hong J, Smith LE, Almeida DM, Coe C, Stawski RS, "Maternal Cortisol Levels and Behavior Problems in Adolescents and Adults with ASD," Journal of Autism and Developmental Disorders, vol. 40, no. 4, pp. 457-69, 2010. DOI: 10.1007/s10803-009-0887-0

[29] Flinn MV, "Evolution and ontogeny of stress response to social challenges in the human child," Developmental Review, vol. 26, no. 2, pp. 138-174, 2006. DOI: 10.1016/j.dr.2006.02.003

[30] Noushad S, Ahmed S, Ansari B, Mustafa UH, Saleem Y, Hazrat H, "Physiological biomarkers of chronic stress: A systematic review," International Journal of Health Sciences (Qassim), vol. 15, no. 5, pp. 46-59, 2021. https://pubmed.ncbi.nlm.nih.gov/34548863/

[31] Bin Eid W, Lim M, Gabrieli G, Kädbel M, Halstead E, Esposito G, Dimitriou D, "Alterations in Cortisol Profiles among Mothers of Children with ASD Related to Poor Child Sleep Quality," Healthcare (Basel), vol. 10, no. 4, pp. 666, 2022. DOI: 10.3390/healthcare10040666

[32] De Andrés-García S, Moya-Albiol L, González-Bono E, "Salivary cortisol and immunoglobulin A: Responses to stress as predictors of health complaints reported by caregivers of offspring with autistic spectrum disorder," Hormones and Behavior, vol. 62, no. 4, pp. 464-474, 2012. DOI: 10.1016/j.yhbeh.2012.08.003

[33] n.d, "Rights of Persons with Disabilities Bill - 2016 Passed by Parliament,"https://pib.gov.in/newsite/printrelease.aspx?relid=155592 (accessed Jan. 21, 2024).

[34] Gaikwad L, Lagala S, "Prevalence and correlates of neurodevelopmental disorders among children in India: a narrative review," International Journal of Contemporary Pediatrics, vol. 8, no. 1, 2020. DOI: 10.18203/2349-3291.ijcp20205438

[35] Hopkins RW, Kilik LA, "The Kingston caregiver stress scale (KCSS) 2016," ProvidenceCare, https://providencecare.ca/wp-content/uploads/2016/10/KCSS-Assessment- Form.pdf (accessed Jan. 21, 2024).

[36] Wilod Versprille LJF, van de Loo AJAE, Mackus M, Arnoldy L, A L Sulzer T, Vermeulen SA, Abdulahad S, Huls H, Baars T, Scholey A, Kraneveld AD, Garssen J, Verster JC, "Development and Validation of the Immune Status Questionnaire (ISQ)," International Journal of Environmental Research and Public Health, vol. 16, no. 23, pp. 4743, 2019. DOI: 10.3390/ijerph16234743

[37] Mauricio Del Rio J, Nicoara A, Swaminathan M, "Neuroendocrine stress response: implications for cardiac surgery-associated acute kidney injury," Romanian Journal of Anaesthesia and Intensive Care, vol. 24, no. 1, pp. 57-63, 2017. DOI: 10.21454/rjaic.7518.241.hav

[38] Anderson HL, Brodsky IE, Mangalmurti NS, "The Evolving Erythrocyte: Red Blood Cells as Modulators of Innate Immunity," Journal of Immunology, vol. 201, no. 5, pp. 1343-1351, 2018. DOI: 10.4049/jimmunol.1800565

[39] Kiecolt-Glaser JK, Glaser R, Shuttleworth EC, Dyer CS, Ogrocki P, Speicher CE, "Chronic stress and immunity in family caregivers of Alzheimer's disease victims," Psychosomatic Medicine, vol. 49, no. 5, pp. 523-535, 1987. DOI: 10.1097/00006842-198709000-00008

[40] Roth DL, Sheehan OC, Haley WE, Jenny NS, Cushman M, Walston JD, "Is Family Caregiving Associated With Inflammation or Compromised Immunity? A Meta-Analysis," Gerontologist, vol. 59, no. 5, pp. 521-534, 2019. DOI: 10.1093/geront/gnz015

[41] Romero-Martínez Á, Moya-Albiol L, "Stress-Induced Endocrine and Immune Dysfunctions in Caregivers of People with Eating Disorders," International Journal of Environmental Research and Public Health, vol. 14, no. 12, pp. 1560, 2017. DOI: 10.3390/ijerph14121560

[42] Ianni CM, McDowall MP, Zuska IA, "Differential Diagnosis of Low Hemoglobin," Dimensions of Critical Care Nursing, vol. 40, no. 4, pp. 204-209, 2021. DOI: 10.1097/DCC.0000000000000483

[43] Irwin MR, "Human psychoneuroimmunology: 20 Years of discovery," Brain Behaviour and Immunity, vol. 22, no. 2, pp. 129-139, 2008. DOI: 10.1016/j.bbi.2007.07.013

[44] Agbayani CJ, Tucker JA, Nelson EL, Martinez F, Cortes H,

Khoury D, Kain ZN, Lin C, Torno L, Fortier MA, "Immunological and psychosocial functioning in parents of children with cancer," Official Journal of the Multinational Association of Supportive Care in Cancer, vol. 30, no. 4, pp. 3379-3388, 2022. DOI: 10.1007/s00520-021-06770-0

[45] Whittaker AC, Gallagher S, "Caregiving alters immunity and stress hormones: a review of recent research," Current Opinion in Behavioural Sciences, vol. 1, no. 28, pp. 93-97, 2019. DOI: 10.1016/j.cobeha.2019.02.002.

[46] Bevans MF, Ross A, Wehrlen L, Klagholz SD, Yang L, Childs R, Flynn SL, Remaley AT, Krumlauf M, Reger RN, Wallen GR, Shamburek R, Pacak K, "Documenting stress in caregivers of transplantation patients: initial evidence of HPA dysregulation," Stress, vol. 19, no. 2, pp. 175-184, 2016. DOI: 10.3109/10253890.2016.1146670

[47] Stalder T, Tietze A, Steudte S, Alexander N, Dettenborn L, Kirschbaum C, "Elevated hair cortisol levels in chronically stressed dementia caregivers," Psychoneuroendocrinology, vol. 47, pp. 26-30, 2014. DOI: 10.1016/j.psyneuen.2014.04.021

[48] Hastings RP, "Child behaviour problems and partner mental health as correlates of stress in mothers and fathers of children with autism," Journal of Intellectual Disability Research, vol. 47, no. 4-5, pp. 231-237, 2003. DOI: 10.1046/j.1365-2788.2003.00485.x

[49] Davis NO, Carter AS, "Parenting Stress in Mothers and Fathers of Toddlers with Autism Spectrum Disorders: Associations with Child Characteristics," Journal of Autism and Developmental Disorders, vol. 38, no. 7, pp. 1278-1291, 2008. DOI: 10.1007/s10803-007-0512-z

[50] Gupta VB, "Comparison of Parenting Stress in Different Developmental Disabilities," Journal of Developmental and Physical Disabilities, vol. 19, no. 4, pp. 417-425, 2007. DOI: 10.1007/s10882-007-9060-x

[51] Miodrag N, Hodapp RM, "Chronic stress and health among parents of children with intellectual and developmental disabilities," Current Opinion in Psychiatry, vol. 23, no. 5, pp. 407-11, 2010. DOI: 10.1097/YCO.0b013e32833a8796

[52] Ranganathan M, Jacon A, Mohammed Ashraf AK, Kumar G, Anthony M, Vijay M, Kumari RB, Annapally SR, "An Investigation of the Effects of Chronic Stress on Attention in Parents of Children with Neurodevelopmental Disorders," Universal Journal of Public Health, vol. 12, no. 1, pp. 37-50, 2024. DOI: 10.13189/ujph.2024.120104.

[53] del Valle Chacin Fuenmayor M, Chacin de Fernandez J, "Psychological Intervention Based on Psychoneuroimmunology in Children and Adults," In Health-Related Quality of Life - Measurement Tools, Predictors, and Modifiers, IntechOpen, 2022. DOI: 10.5772/intechopen.92935