Relationship between perceived academic stress and Interleukin 6 levels in health students

Relación entre el estrés académico percibido y los niveles de Interleucina 6 en estudiantes de salud

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ABSTRACT

Background: Academic stress is an important research topic due to the effect it has on the quality of life of students, future professionals and therefore, adult contributors in a society. It has been shown that students in the health field face additional stressors specific from their careers, and suffer greater stress than the general population of the same age. **Methods:** 52 students, 23 from Physiotherapy and 29 from Medicine programs were surveyed with Academic Stressors Academic Scale (SAS) to know academic stress level and IL-6 was quantified in serum. **Results:** It was found that students who perceive the academic semester as stressful "fairly often" and "many times", increases in 50%, 75% and 76.9% during the semester; while "anxiety/distress" feeling was predominant. The most frequent SAS scale factors were "methodological deficiencies", "student overload", "beliefs about performance", "lack of content value", "participation" and "exams" **Conclusion:** The study revealed an IL-6 increment, and their association with "Methodological Deficiencies" at 1st moment. This study showed the importance of academic stressors identification at same time that it is a call to construct strategies to reduce stressors in University context.

Keywords: Academic stress; IL-6; Physiotherapy; Psychoneuroimmunology.

Introducción: El estrés académico es un tema de investigación importante debido al efecto que tiene sobre la calidad de vida de los estudiantes, futuros profesionales y, por lo tanto, los contribuyentes adultos en una sociedad. Se ha demostrado que los estudiantes en el campo de la salud enfrentan factores estresantes adicionales específicos de sus carreras y sufren un mayor estrés que la población general de la misma edad. **Métodos:** 52 estudiantes, 23 del programa de fisioterapia y 29 del programa de medicina fueron encuestados con la Escala de Estresores Académicos del Cuestionario de Estrés Académico (E-CEA) para conocer el nivel de estrés de los estudiantes; la citoquina IL-6 se cuantificó en suero. **Resultados:** Se encontró que la frecuencia de estudiantes que perciben el semestre académico como estresante "con bastante frecuencia" y "muchas veces", aumenta en un 50%, 75% y 76.9% durante el semestre; mientras que el sentimiento de "ansiedad / angustia" era predominante. Los factores de la escala E-CEA más frecuentes fueron "deficiencias metodológicas", "sobrecarga de estudiantes", "creencias sobre el rendimiento", "falta de valor de contenido", "participación" y "exámenes". **Conclusiones:** El estudio reveló un incremento de IL-6 y su asociación con "Deficiencias metodológicas" en el 1er momento. Este estudio mostró la importancia de la identificación académica de estresores al mismo tiempo que hace un llamado a construir estrategias para reducir los estresores en el contexto universitario.

Palabras clave: Estrés académico; IL -6; Fisioterapia; Psiconeuroinmunología

I. INTRODUCTION

Academic stress is an important research topic due to the effect it has on the quality of life of students, future professionals and therefore, adult contributors in a society. It has been shown that students in the health field face additional stressors specific from their careers, and suffer greater stress than the general population of the same age (1, 2). Among these stressors have been mainly identified, the awareness of having in their hands people's health and life, extended work hours, difficult work places (emergency rooms or intensive care) and continuous assessment of large volumes of knowledge. In response to these stress circumstances, students can develop depression (3) drug dependence (4), suicidal tendencies (5), difficulty in establishing interpersonal relationships (6), as well as associated pathologies such as musculoskeletal disorders (7), infections (8), oral diseases (9), and autoimmune disorders (10), among others. Research on the association between stress and students in health areas is extensive (11-13). Survey-type tools to elucidate the problem qualitatively, have noted that time available to perform academic activities, fear of failure, interactions within the classroom, economic problems and social and global problems, are the most frequent stressors within this population, while the consequences are associated with these factors: high burnout index, fatigue and depersonalization, emotional exhaustion, depression and suicidal ideation (14).

Of these studies, few inquire students' health status through their own biological indicators for this purpose. In this sense, the relationship between stress and the immune system has been explored; for example, it has been shown that in situations of acute stress, health science undergraduate students have an increase in the concentration of cortisol in their blood (15), leukotriene in nasal fluids (16). It is also related to an increase of the adrenocorticotropic hormone (ACTH), which in turn generates an increase in the IL-4, IL-10 and IL-13 cytokines that have anti-inflammatory effects, and a decrease in the pro-inflammatory IL-1β, IL-6, TNF-α, IFN-γ, IL-2 and IL-12 cytokines (17). On the other hand, when stress is chronic, fatigue of the hypothalamus-adrenal pituitary axis occurs, which attenuates the response of cortisol, causing resistance to glucocorticoids due to the low expression of its receptors; therefore, the effect of cortisol on the inflammatory response loses its effect and increases IL-6, TNF-α and IFN-γ levels (18), so that chronic stress is related to a pro-inflammatory profile (19), which can become an etiological factor of pathologies of an inflammatory nature.

Considering the above, this research aimed to identify the circumstances of academic stress in a population of Physiotherapy and Medicine students of the Faculty of Health Sciences of the University, through the application of the Academic Stressors Scale *SAS* and the pro-inflammatory cytokine IL-6 quantification.

II. METHODS

Study population. An observational, longitudinal and descriptive study was carried out. The selected population was obtained from the students of the Faculty of Health Sciences of the University, enrolled in the seventh semester of the Medicine Program and from the sixth semester of the Physiotherapy Program; who were chosen due to their higher academic load according to their study plans. The following aspects were taken into account as inclusion criteria: Academic enrollment with 100% of the academic credits required for the corresponding semester, signature of the informed consent, presence in the three moments of the survey administration and in peripheral blood samples collection, students who were not consuming any type of drugs or hallucinogenic substances, and as an indication of the peripheral blood

samples collection, who had followed a minimum fast of 8 hours. 52 students participated, 23 students from the Physiotherapy Program and 29 students from the Medicine Program; however, the quantification analysis of IL-6 was performed on 51 students given the dispersion of 1 case between the first and the second moment. All the procedures were approved by the Ethics Committee of the University, the project was registered with ID 4624 in the Research System of the University.

Measurement of stressors. The stressors were measured through a survey of sociodemographic characteristics and the academic stressors questionnaire, which was formulated and validated in 2016 by Cabanach and collaborators (reliability of a=0.96) (20). From this questionnaire, the Stressors Academic Scale (*SAS*) was used, consisting of 54 questions with Likert-type answers (Never =1, Sometimes= 2, Fairly Often =3, Many times =4 and Always =5). The survey was first administered on the first week of the semester ("*1st Moment*"), where the survey of sociodemographic characteristics (age, gender, socioeconomic status, marital status, economic stability and academic program) was also administered. The survey was administered again in week 13, where the 70% evaluation of the academic content takes place, and in week 16, where final exams are taken, defined as the "*2nd Moment*" and the "*3rd Moment*", respectively. The *SAS* was entirely assessed and grouped into 8 factors: teacher's methodological deficiencies (12 items); student's overload (10 items); public interventions (5 items); bad social relationships in the academic context (6 items); lack of control over one's academic performance (5 items); lack of content value (4 items); low academic esteem (5 items); exams (4 items); inability to participate in decisions regarding one's own academic work (3 items).

IL-6 determination in serum of peripheral blood. IL-6 determination in serum of peripheral blood was performed by means of peripheral venous blood samples, which were obtained by direct venipuncture with the Venoject system (Terumo Europe NV Eschborn Germany), using Vacutainer® tubes without additives (BD Franklin Lakes red cap tubes, NJ, USA). 6 mL of blood was collected from each person in the established times (1st, 2nd and 3rd moments). The serum was separated by centrifugation and the samples were labeled and stored at -70°C until the cytokine IL-6 was quantified. The cytokine IL-6 was quantified from peripheral blood serum by the sandwich ELISA method using the Human IL-6 ELISA MAX™ kit (Biolegend), the procedure was performed according to the manufacturer's instructions.

Data analysis. The data from the *SAS* and the Cytokine IL-6 quantification were included in an Excel-type electronic sheet in which each student was assigned a code; once the data were entered, the electronic sheet was exported to the statistical program SPSS.19 for its corresponding analysis. The sociodemographic variables were analyzed using frequency and percentage tables, as well as the variables of the academic stressor questionnaire, which were analyzed first by question and then by groups or factors, comparing the average behavior by factor in each of the programs. To classify the results by average, it was decided to group them in ranks to facilitate the interpretation of the final results: 0 to 0.9 "Never", 1 to 1.9 "Sometimes", 2 to 2.9 "Fairly often", 3 to 3.9 "Many times" and 4 to 5 "Always". Finally, the questionnaire questions which presented the highest response rate represented in the final average were selected; as a selection criterion, it was taken into account that the question obtained a frequency greater than or equal to 20 in the answers, except for the ones answered as "never", and that it would be repeated in the results of each moment of the questionnaire administration. For the analysis of the IL-6 quantification, the ANOVA test was performed for repeated samples and the Dunn's multiple comparison test, with a value of $p \leq 0.05$. Finally, a Pearson correlation

was conducted between the higher frequency academic stressors by academic program and the IL-6.

III. RESULTS

Analysis of socio-demographic variables. The average age of the surveyed students was 21.54 years, with a minimum age of 19 years and a maximum of 27 years; 38.5% (20/52) of the respondents were men, while 61.5% (32/52) were women; regarding the socioeconomic level classificated in Colombia by 5 strata, being stratum 1 the lowest income and stratum 5 the highest income; 78.8% (41/52) belonged to 1, 2 and 3 strata. 73.1% (38/52) considered having a good economic stability. Regarding marital status, 98.1% (51/52) reported being single. Among the respondents, 44.2% (23/52) were enrolled in the Physiotherapy program and 55.8% (29/52) in the Medicine program. **Table 1** describes the socio-demographic characteristics.

Table 1. Bivariate analysis of the socio-demographic variables of Physiotherapy and Medicine students.

VARIABLE	PHYSIOTERAPY n (%)	MEDICINE n (%)
Age	21.54±v2.8	21±1.6
Gender		
Male	6 (26.1)	14 (48.3)
Female	17 (73.9)	15 (51.7)
Socioeconomic stratum		
One	6 (26.1)	0 (0)
Two	8 (34.8)	8 (27.6)
Three	6 (26.1)	13 (44.8)
Four	3 (13.0)	7 (24.1)
Five	0 (0)	1 (3.4)
Marital status		
Single	22 (95.7)	29 (100)
Common law marriage	1 (4.3)	0 (0)
Economic stability		
Regular	6 (26.1)	7 (24.1)
Good	16 (69.6)	22 (75.9)
Excellent	1 (4.3)	0 (0)

Source: own elaboration

Analysis of the survey on perceived academic stress

Regarding the level of perceived stress, it was found that at the *1st moment* 48.1% (25/52) perceive stress "sometimes", however 50% (26/52) perceive it "fairly often" and "many times".

When administering the survey at the *2nd moment*, the level of stress perceived by the students was 75% (44/52) for a stress level between "fairly often" and "many times", as well as the level of stress perceived by students at the *3rd moment* with a percentage of 76.9% (27/56). Having said that, regarding the predominant feeling, the "anxiety / distress" was the main emotion that produced stress, this tendency was reiterative in the three moments of the study.

Concerning the factors of the *SAS* survey, it was found that in the studied population, 6 out of 8 factors, namely "methodological deficiencies", "student's overload", "beliefs about one's academic performance", "lack of content value", "participation" and "exams", presented a rising variability, in the three moments of the study, going from experiencing stress manifestations "sometimes" to "fairly often" (**Table 2**).

Table 2. Average of each *SAS* factor for academic programs

FACTOR	1st MOMENT $\overline{x} \pm DE$	2nd MOMENT $\overline{x} \pm DE$	3rd MOMENT $\overline{x} \pm DE$
Methodological deficiencies	2.9 ± 0.8	3.0 ± 0.8	3.1 ± 0.9
Student overload	30 ± 0.8	3.3 ± 0.9	3.3 ± 0.9
Beliefs about performance	2.7 ± 0.8	2.9 ± 0.9	3.1 ± 1.0
Public interventions	2.7 ± 0.9	2.6 ± 0.8	2.7 ± 0.8
Negative social climate	2.1 ± 0.9	2.0 ± 0.8	2.2 ± 0.9
Lack of content value	2.4 ± 0.9	2.6 ± 0.9	2.8 ± 1.0
Participation	2.0 ± 0.7	2.2 ± 0.9	2.6 ± 0.9
Exams	3.0 ± 0.9	3.1 ± 0.8	3.4 ± 0.9

Quantitative and qualitative values of academic stressors according to the *SAS*. 0-0.9 = never; 1.0-1.9 = Sometimes; 2.0-2.9 = Fairly often; 3.0-3.9 = Many times; 4.0-5 = Always
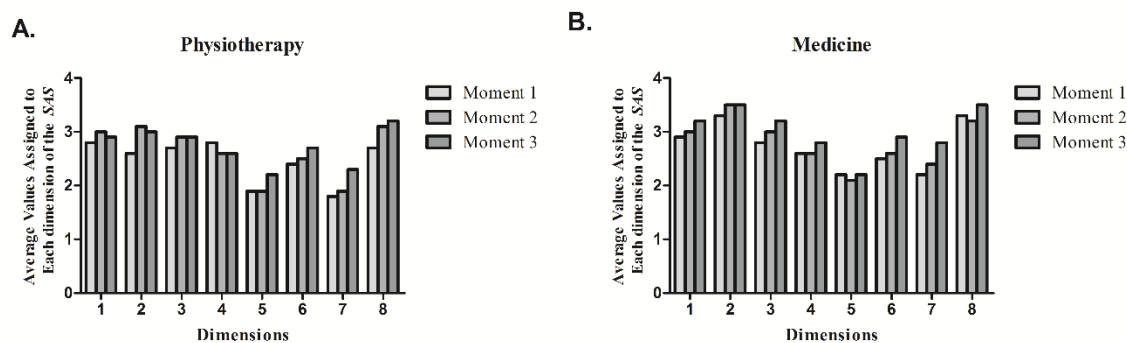**Source:** own elaboration

The comparison of means for each factor in the Physiotherapy and Medicine academic programs is described in **Figure 1**; it was found that the "academic overload" is a prevalent factor with greater response to stress in the Medicine students than in the Physiotherapy students, another factor affected through the academic semester is the one corresponding to "exams", being higher the frequency of stressors in Medicine students. **Figure 1** shows the perception of the different stressors in the students by academic program, where it is evident that the Medicine students exhibit greater perception in the *SAS* academic stressors. The "activity overload", "exams", "beliefs about performance" and "methodological deficiencies" means values are the three factors with the highest stress load perceived by Medicine students with a "fairly often" value above 3, while the factor perceived as the most stressful in the Physiotherapy program was "exams".

Levels of IL-6 in serum in physiotherapy and medicine students

When performing the descriptive analysis of the IL-6 concentration behavior in the serum of students, it was observed that the data median increased progressively at each moment (**Table 3**).

Figure 1. Averages comparison for each *SAS* factor by academic program.

Source: Own elaboration

The data represent the means by factors relating to: 1. Methodological deficiencies; 2. Student Overload; 3. Beliefs About Performance; 4. Public Interventions; 5. Negative Social Climate; 6. Lack of Content Value; 7. Participation; 8. Exams. The values were represented as 0-0.9 = never; 1.0-1.9 = Sometimes; 2.0-2.9 = Fairly often; 3.0-3.9 = Many times; 4.0-5 = Always.

Table 3. Descriptive values of the IL-6 quantification in Medicine and Physiotherapy students during the academic semester

	1st Moment	2nd Moment	3rd Moment
Sample size	51	51	51
Minimum value	0.0	0.05	1.9
Percentile 25	1.15	2.15	5.25
Median	3.8	5.1	10
Percentile 75	6.9	9.9	14.6
Maximum value	37.05	44.9	54.4

Source: Own elaboration

When the ANOVA test for repeated samples and the Dunn's multiple comparison test were performed, a significant difference was shown in the IL-6 production between the *1st moment* and the *3rd moment*. Likewise, a significant difference was shown between the *2nd moment* and the *3rd moment* (**Figure 2**). The above shows that, at a general level, the students of the Physiotherapy and Medicine programs suffered an increase of this pro-inflammatory cytokine during the academic semester.

Figure 2. IL-6 quantification (pg/mL) in serum of Physiotherapy and Medicine students throughout the academic semester.
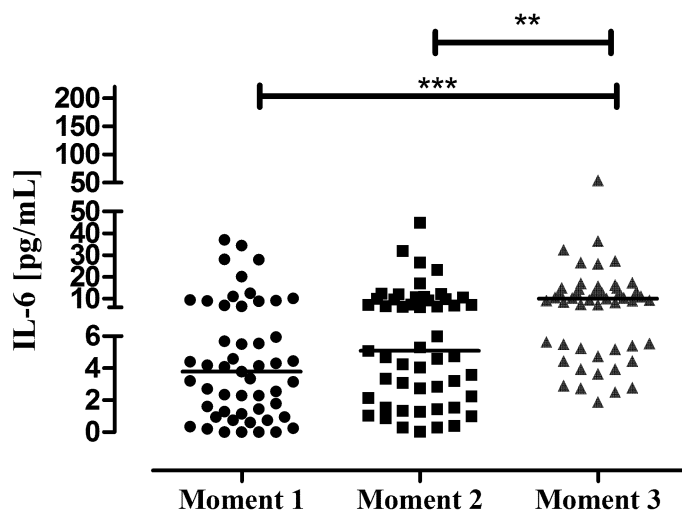
The figure shows the pooled values of the cytokine IL-6 quantification during three moments of the academic semester. The 1st Moment (black circles) corresponding to the beginning of the semester; The 2nd Moment (black squares) corresponding to the 70% grading period of the academic semester; The 3rd Moment (black triangles) corresponding to the end of the semester. The data represent each individual in the study and the horizontal line represents the data median, which were analyzed by the ANOVA test for repeated samples and the Dunn's multiple comparison test, $p < 0.001$ (***) and $p < 0.01$ (**).

Figure 3. IL-6 levels (pg / mL) in serum of Physiotherapy and Medicine students throughout the academic semester
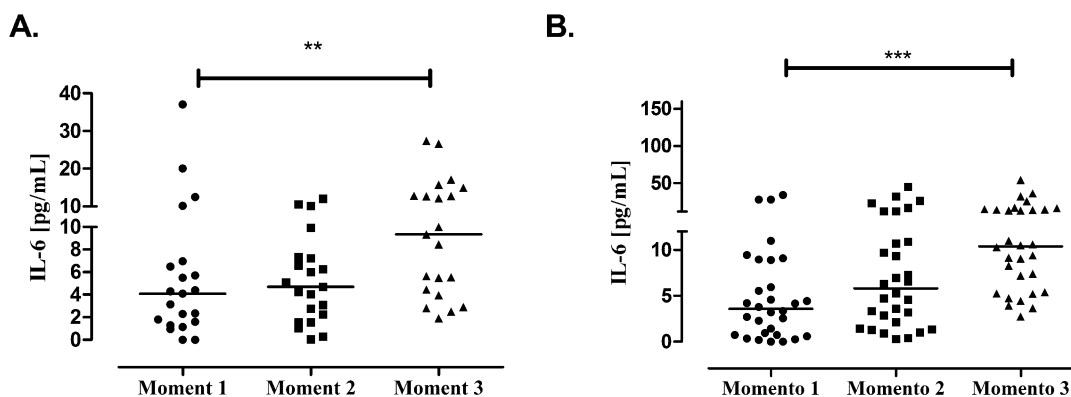
The figure shows the quantification of the Cytokine IL-6 in students of the Physiotherapy program (A) and the Medicine program (B) during three moments of the academic semester. The *1st Moment* (black circles) corresponding to the beginning of the semester; the *2nd Moment* (black squares) corresponding to the 70% grading period of the academic semester; the *3rd Moment* (black triangles) corresponding to the end of the semester. The data represent each individual in the study and the horizontal line represents the data median, which were analyzed by the ANOVA test for repeated samples and the Dunn's multiple comparison test, $p < 0.001$ (***) and $p < 0.01$ (**).

When analyzing the IL-6 production in each program, it was observed that the Physiotherapy program students do not show significant changes in the IL-6 production between the first and the second moment, even though the values show a relative increase. However, between the *1st moment* and the *3rd moment* a significant increase is shown (**Figure 3.A**). Regarding the Medicine program students, a significant increase was observed between the *1st moment* and the *3rd moment* (**Figure 3.B**). These results reflect that the IL-6 values increase progressively throughout the semester, both in the Physiotherapy program and in the Medicine program, according to the behavior of the grouped data.

Correlation between the *SAS* survey results and the IL-6 production

When analyzing the overall correlation between *SAS* factors and the IL-6 quantification for each moment, an association was found in the Methodological Deficiencies factor with a 0.78 value at the *1st moment*, in the other factors there was no correlation among the variables (**Table 4**).

Table 4. Correlation for each factor of the *SAS* survey and the cytokine IL-6 quantification in the students of the Physiotherapy and Medicine academic programs

Factor	IL-6		
	1st Moment	2nd Moment	3rd Moment
Methodological deficiencies	0.78*	-0.58	-0.123
Student overload	-0.52	-0.15	-0.127
Beliefs about performance	0.006	0.086	-0.128
Public interventions	-0.145	-0.104	-0.114
Negative social climate	0.15	0.124	-0.136
Lack of content value	0.151	-0.05	-0.113
Participation	0.29	0.019	-0.106
Exams	-0.136	-0.103	-0.257

* A correlation of ≥ 0.3 with p value ≤ 0.05 is considered significant
Source: own elaboration

The situational stimuli that the students rated as more threatening for each of the *3 moments* were correlated with the IL-6 production and no significant relationship was found (data not shown).

IV. DISCUSIÓN

The students who participated in the study share similar sociodemographic characteristics and are enrolled in the semester with the highest number of academic credits of each program. When investigating the level of perceived stress in the population, it was observed that as academic semester progresses, the level of perceived stress by the students was higher, characterized by an anxiety and distress feeling; however, a scale was not applied to determine such levels of anxiety (21).

Regarding the *SAS* survey factors, it was found that in studied population (6 out of 8), factors such as: "methodological deficiencies", "student overload", "beliefs about performance", "lack of content value", "participation" and "exams", presented variability in the three moments of the survey administration. Though, Medicine students showed greater stressors in the "Academic overload", "Methodological deficiencies" and "Exams" factors; similar to what was found in the study by Taboada *et al.,* 2015 (22) who found that university students are "fairly often" stressed by situations related to the factors corresponding to "methodological deficiencies", "academic overload" and "exams", which, corresponds to the results obtained by this investigation. Meanwhile, in Physiotherapy students the factors with the most frequent stressors were: "Academic overload" and "exams". The results presented in this study agree upon the results obtained by Toribio *et al.,* 2016, who studied a population of undergraduate nursing students at the University of Papaloapan (Mexico), where he found that the most affecting stressors in this population were: "exams", "academic overload", "short delivery period" and "teacher's personality / character" (23).

Regarding the "exams" factor, which is perceived as an important stressor and is related both, to its preparation and its proximity or administration of the exam, it has been determined that is the one that produces greater anxiety and tension, for this reason it is assigned an important role as a trigger for a state of emotional stress associated with the action of taking exam. The result of this study, just like that of Hernández *et al.,* 2011 (24), show that anxiety about exams not only affects academic performance, but is also related to the emotional state and students' health. The obtained results were corroborated with the results of other investigations (25, 26) and are coherent with the related studies in the corresponding subject. That is, "exams" and "academic overload" are among the most frequent academic stressors in the life of a university student.

Regarding the "participation" factor, this study shows that what affects students the most is giving an oral presentation about their work, or expressing themselves to others during a certain period of time, as well as answering questions, expressing opinions or explaining their point of view to the audience. These stress situations may have their origin in the quality of the academic preparation to be presented, or in a personal insecurity. Thus, it can be concluded that students perceive as stressful, any situation in which they are evaluated through participation, these findings are similar to those reported by García *et al.,* 2014 (26). In our study, the "participation" factor is classified as a stressor that can have a negative impact on the health of university students. The participation situations that affect students the most are giving an oral presentation about their work or expressing themselves to others. In the "negative social climate" factor, students perceive an uncomfortable environment within their respective classrooms, which hinders peer support and collaboration. This factor can be explained related to the natural grouping constituted by the classroom and the interactions taking place in it through cooperation, competition or leadership, and which configure what we know as social climate, which can be explained with the time students spend throughout their academic

training in both, theoretical, and practical activities; these academic stressors were assessed with a "many times" occurrence, but in spite of this, no significant differences were found, similar to what was found in the study by García et al., 2014, where the least stressful factor was "the negative social climate" perceived by students in Health programs (26).

Cytokine profiles are immune-biochemical markers frequently used in stress situations. Studies have shown relationship between problems associated with stress with pro-inflammatory cytokines increase in patients, for example in the meta-analysis conducted by Segerstrom & Miller (2004) (27), it was found that in patients with psychological stress, there is a high concentration of cytokines such as IFN-γ and IL-6. This increase in pro-inflammatory cytokines has also been documented in studies where circumstances of academic stress were evaluated in students of Health Sciences programs (28). Our results show an increase of the cytokine IL-6 when analyzing the grouped data of the students of the Physiotherapy and Medicine programs; this increase appears when comparing three moments of the academic semester, being significant the difference between the first and the third moment, and between the second and the third moment. These data correlate with the ones reported by different authors (29, 30). Likewise, Marshall *et al.*, 1998 analyzed the IFN-γ and IL-10 levels, four weeks before and 48 hours after a partial exam in 16 Medicine students at the University of Texas; results showed higher IFN-γ values before the test, which decreased after 48 hours, while the IL-10 values increased. These data suggest that "exams" situation is psychologically stressful, and changes the balance of Th1/Th2 type cytokines, causing the Th2 type content to increase, which produces an immunological dysregulation (31). Similarly, Lester *et al.,* 2010, analyzed the concentrations of various cytokines, including IL-6, in saliva samples from 36 Anatomy students from different programs in the health area one day before the 3 evaluations of the semester, the results showed that IL-6 concentrations as well as other pro-inflammatory cytokines increased gradually from the first evaluation to the third one (32).

Increase of the IL-6 in Physiotherapy and Medicine students should be taken into account as a starting point to conduct new studies to evaluate the immune status of students, since it has been suggested that the changes evidenced in the balance between Th1/Th2 responses, could lead to a decrease in cell-mediated immunity, which would increase the risk of susceptibility to viral, mycotic and bacterial infections (33, 34); at the same time, chronic increase of the cytokine IL-6 could be related to short, medium or long term development of diseases of inflammatory etiology, such as cardiovascular diseases, diabetes, obesity, periodontal diseases, even cancer (35, 36).

In addition, the chronic inflammatory condition, not only would be related to the physical health of students, but also to their mental health, since the inflammation affects several neurotransmitter systems in the brain, including the serotonin, dopamine and glutamate pathways, as well as to the kynurenine pathway, which generates quinolinic acid, a neurotoxic metabolite. Neuroimaging studies have shown that disruption of neurotransmitter pathways is associated with inflammation-induced alterations in brain circuits that mediate motivation and motor activity, as well as anxiety, activation and alarm (37), so that eventually this chronic inflammatory process caused by academic stress could converge in depression (38).

Regarding the correlation between *SAS* factors and the cytokine IL-6, it was only found correlation in the "1st Moment", specifically in the "methodological deficiencies" factor (0.78) In this regard, authors such as Taboada 2015, express a relationship between academic performance and stress expressed by students, with the disparity between what the teacher teaches and how he/she evaluates (22). Several studies have addressed the teaching-learning

process itself as one of the most significant stressors, mainly related to teacher-student relationships, so it is striking how this strong relationship appears at the beginning of the academic semester before formally starting classes. Undeniably, the difficulties derived from this poor teacher-student interaction are sources of instability, imbalance and academic tensions (23, 26). Nevertheless, no significant correlations were found between *SAS* factors and IL-6; this concurs with the study by Koh *et al.,* 2012 (39) who analyzed effects of psychological stress and pro-inflammatory and anti-inflammatory (IL-6, TNF-α) cytokines in Medicine students. In this case, they did not find a significant relationship between the results of survey and those of the cytokines; still, independently, significant data related to academic stress circumstances were found.

Despite having a measurement scale of academic stressors such as *SAS*, an instrument that allowed to evaluate specific factors to qualify the perception of students' academic stressors, when correlating them with the biological IL-6 measurements, it was observed an absence of equivalence between scale and biological measure as expressed by Tangarife-Lujan and Cardona Arias (40).

CONCLUSIONS

This study revealed that the greatest stressors perceived with the *SAS* survey administration in the Medicine and Physiotherapy students were (6 out of 8): "methodological deficiencies", "student overload", "beliefs about performance", "lack of content value", "participation" and "exams", these presented a rising stress variation, in the three moments of the study, going from presenting stress manifestations "Sometimes" to "Fairly often".

The study revealed an association between IL-6 values and methodological deficiencies in the evaluation of academic stress level. There was no correlation between the other *SAS* factors and the IL-6 quantification in students of the Faculty of Health Sciences of the University, probably due to the absence of equivalence between the scale and the biological measure. However, the obtained results show that, independently, there is an increase in the cytokine IL-6 over time during the academic semester and that the *SAS* scale serves to identify the main stressors of students.

This study showed the importance of academic stressors identification to mark a roadmap for the close support of students who experience stress, at same time as it calls for strategies to reduce stressors in University context.

In addition, this study shows the progressive increase of interleukin-6 during a state of chronic academic stress, which correlates with the evidence of the relationship between inflammation and psychiatric illness. Because there is also a relationship between inflammation and progression of different diseases, knowing the inflammatory state of people who experience stress is an interesting topic to explore and prevent diseases linked to chronic inflammatory processes.

Authors contribution: "Conceptualization, Julio Klinger; methodology, Paola Vernaza, Victoria Niño.; software, Jayson Chavarria; validation, Gloria Ávila González.; formal analysis, Jerónimo Londoño, Paola Vernaza, Victoria Niño; research, Paola Vernaza; resources, Victoria Niño.; data healing, Paola Vernaza. writing: preparation of original draft, Jayson Chavarria; writing: review and editing, Paola Vernaza.; viewing, Jerónimo Londoño.; supervision, Rosa Dueñas Cuellar.; project management, Paola Vernaza, Jerónimo Londoño, Rosa Dueñas,

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