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Medication-Taking Self-Efficacy

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Discovering Thoughts, Inventing Future

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Maternal Child Feeding Practices: Relationship with the BMI and Body Fat Percentage of Mexican Children

By Flores-Peña, Yolanda, Avila-Alpirez, Hermelinda, Trejo-Ortiz, Perla M., Mercedes Gutiérrez Valverde, Roxana Araujo Espino & Gustavo Gutiérrez Sánchez
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Abstract- *Objectives:* 1) To assess the reliability of the Child Feeding Questionnaire (CFQ), 2) To describe maternal child feeding practices (MCFP) and 3) To associate the MCFP with the child's body mass index (BMI) and body fat percentage (BFP).

Methods: A cross-sectional correlational study. Participants: 786 pairs (mother and preschooler / schooler child). The mothers answered the CFQ, which consists of 31 items, distributed among seven factors. The mother's and child's weight and height were measured, and the child's BFP. Descriptive statistics and Spearman's correlation coefficient were applied.

Results: The CFQ obtained a 0.75 Cronbach's alpha coefficient, 283 children (36.01%) were overweight or obese, BFP mean was 25.90 (SD = 9.92) for boys and 27.20 (SD = 8.79) for girls. Related to MCFP, the perceived responsibility factor obtained the highest score (Mean = 84.35, SD = 16.99), while the lowest scores were for perceived child weight (Mean = 50.06, SD = 8.38) and concern about child weight (Mean = 44.69, SD = 29.34). The factor, perceived child weight was associated with the child's BMI ($r_s = 564$, $p = .001$) and BFP ($r_s = 535$, $p = .001$).

Keywords: *maternal feeding practices, overweight, obesity, weight perception, mother-child relations.*

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Flores-Peña, Yolanda [α], Avila-Alpirez, Hermelinda [σ], Trejo-Ortiz, Perla M. [ρ], Mercedes Gutiérrez Valverde [Ꞷ], Roxana Araujo Espino [¥] & Gustavo Gutiérrez Sánchez [§]

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Conclusions: The internal consistency of the CFQ was acceptable. The mothers considered themselves responsible for their child's feeding, although the child's weight didn't represent a concern. Interventions are recommended to help the mother accurately perceive their child's weight.

Keywords: maternal feeding practices, overweight, obesity, weight perception, mother-child relations.

I. Introduction

Childhood obesity is one of the most severe public health problems of the 21st century(1). Its prevalence has increased at an alarming rate. Around the world, 41 million children suffer from overweight (OW)-obesity (OB). The problem is global and is steadily affecting many low- and middle-income countries, particularly in urban settings (1).

The increased prevalence of childhood OW-OB is a situation with multiple intervening factors, including genetic factor, reduction of physical activity, increased calorie intake, in addition to parents' traditional false beliefs about health and nutrition (2). On the other hand, research findings have indicated a correlation between maternal behavior and children's adiposity levels (3), as well as a correlation between the maternal child-feeding practices and children's food preferences (4), energy intake, and weight status (5).

The Domain Specific Parenting Styles Model and its impact on the development of childhood OB support the understanding of parents' child feeding practices (6). The authors proposed that parents do not have a single and consistent style to raise their children and suggest that child rearing styles differ among the parents, across the child's development phases and among children in the same family.

Moreover, they assure parents practice higher levels of control on their child's feeding when: a) the parent is concerned with the child's development, b) is closely involved in the child's health, physical wellbeing or weight, c) perceives that the child is at risk of developing feeding and/or weight problems based on the family history and other risk factors, and d) does not believe that the child is capable of self-controlling his diet (6).

To assess parental child feeding practices, different questionnaires have been used, including Comprehensive Feeding Practices Questionnaire (7), Preschooler Feeding Questionnaire (8) and Child Feeding Questionnaire (CFQ) (9). The last one has been used more frequently in research, which consists of 31 items, grouped in seven factors. Four of these factors pertain to parental perception of child and parent weight, and concern about weight, which may elicit parental control in feeding, and three additional factors assess parents' attitudes and practices regarding their use of controlling child feeding strategies (9).

Fathers and mothers of children between two and eleven years of age can answer the CFQ; it's internal reliability coefficient of 0.75 has been found for the total scale (9). Studies conducted in different countries, including China (10), Spain (11), Portugal (12), Sweden

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(13) and Turkey (14) have applied. Until date, any study in Mexican population have applied CFQ.

The literature has reported the association between parental child-feeding practices and child's body mass index (BMI), which is the most frequently used indicator, as well as body fat percentage (BFP). A study involving African-American mothers, and white boys and girls documented that parental child-feeding practices explained up to 15% the child's BFP variance (15).

Given the global increase in the childhood OB prevalence, different factors that could contribute to childhood OW-OB need to be identified, to design effective interventions to reduce and treat this problem. Also, considering that has not been found research that explores the relationship between maternal child feeding practices and child weight in Mexican population, this study was an undertaken, involving pairs (mothers and their preschoolers and schooler children) residing in the northeastern area of Mexico. The objectives were: 1) To assess the reliability of the CFQ, 2) To describe maternal child-feeding practices (MCFP) and 3) To associate the MCFP with child's BMI and BFP.

II. Methods

We conducted a cross-sectional correlational study. Participants were pairs (mother and preschooler / schooler child). The children were healthy, without any growth problems referred by their mothers, and enrolled at six public educative institutions (three kindergartens and three elementary schools). The institutions were randomly selected among the 538 educative institutions of Monterrey, Nuevo Leon metropolitan area. 915 mothers were invited to participate with their child, and 786 pairs (mother - preschooler / schooler child) provided the complete information.

a) *Measurements*

To assess the maternal child feeding practices, the CFQ (9) was applied, which consists of 31 items in seven factors. Four factors are: a) perceived feeding responsibility (PFR), b) perceived parental weight (PPW), c) perceived child´s weight (PCW), d) concern about child´s weight (CCW). Three additional factors evaluate parental attitudes and practices regarding use of control child feeding strategies: a) monitoring of food intake (M), three items. This factor assesses the extent to which parents oversee their child´s eating, supervise the consumption of sweets, snacks, and foods with a high-fat level. Scores range from 1 to 5, low to high monitoring; b) food restriction (R), eight items. This factor assesses the extent to which parents restrict their child´s access to foods. The scores range from 1 to 5, low to high restriction; c) pressure to eat (P), four items. This factor assesses parents' tendency to pressure their child to eat more food, typically at mealtimes. Scores range from 1, for low pressure, to 5 for high pressure.

Reported Cronbach's alpha coefficients for CFQ factors to range between 0.60 and 0.93 (9-11). The CFQ was designed for application to parents of children between two and eleven years of age. Before to applying, the questionnaire was translated into Spanish using a translation-back-translation method.

b) *Anthropometric Measures*

The maternal and children height was measured using a SECA 214 stadiometer. Maternal and, child's weight was measured using SECA 813 scale, with a capacity of 200kg and precision level of 0.1 gr. Then, the maternal BMI was calculated by applying the formula weight/height^2 and classified according to WHO determinations (16) as low weight (<18.5), normal weight (18.5 to 24.9), overweight (25.0 to 29.9) and OB (BMI > 30.0). The child's BMI was classified in percentiles according to WHO standards (17) as malnutrition (percentile <3), low weight (>3 y <15), normal weight (>15 and <85), OW (>85 but < 97) and OB (>97), and the child's BFP was measured by bioelectric impedance using Inbody 230 equipment.

Maternal sociodemographic data were obtained, including age and education in years, occupation, and marital status. Regarding the child, age and gender were obtained.

c) *Data Collection Procedure*

After administrative process, were recruited the participants through meetings, flyers, and take-home letters. The mothers who agreed to participate signed a consent form and answered the CFQ, the time needed to complete it was approximately 15 minutes. Also, socio-demographic data were collected in a self-administered questionnaire, e.g., age, education level, marital status, monthly family income and the child's age and sex. Finally their weight and height were measured. We measured the weight, height, and BFP child' in the educative institution, previous authorization from the teacher responsible for each classroom

This project was approved by School of Nursing Ethical Committee at the Autonomous University of Nuevo León. Mothers gave their informed consent and authorized the participation of their children.

d) *Data Analysis Strategies*

The data were collected and analyzed using the Statistical Package for the Social Sciences (SPSS), version 23. We calculated the Cronbach's alpha for the factors and the total CFQ, and obtained descriptive statistics of the participants' socio-demographic data. The score of each factor and score of the total questionnaire were transformed into rates between 0 and 100, in which a low score indicate a worst MCFP

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and high a better MCFP. The data showed no normal distribution. Therefore Spearman's correlation coefficient was applied to associate the MCFP with the child's BMI and BFP.

III. Results

The internal consistency of the CFQ was verified using Cronbach's alpha for the factors and the total questionnaire. The coefficients for the factors ranged between 0.68 and 0.86; and 0.75 for the total questionnaire (Table 1).

786 pairs (mother and child) participated. The mean maternal age was 34.18 years (SD = 6.79), 62.21% (n = 489) of the mothers had finished junior high school or high school, and 43.89 (n = 345) referred they worked out the home. The 36.77% (n = 289) of the mothers had OW and 28.37% (n = 223) OB.

Concerning children, the mean age was 7.20 years (SD = 2.53), 49.10% (n = 386) were male and 50.90% (n = 400) female, 21.88% (n = 172) was OW and 14.13% (n = 111) OB. The BFP mean was higher among girls (Mean = 27.20, SD = 8.79) than among boys (Mean = 25.90, SD = 9.92), the information is displayed in Table 2.

We calculated rates for the factors and the total questionnaire. Table 2 shows that the highest mean score was found for perceived responsibility (Mean = 84.35, SD = 16.99), followed by monitoring factor (Mean = 71.94, SD = 25.88). The lowest scores were found for concern for child's weight (Mean = 44.69, SD = 29.34) and perceived child's weight (Mean = 50.06, SD = 8.38). The highest correlation was found between child's BMI and perceived child's weight (r_s = 564, p = .001), and between perceived child's weight (r_s = 435, p = .001) and child's BFP, data shown in Table 4.

IV. Discussion

The CFQ is one of the most used questionnaires to assess parental child feeding practices. In a study involving fathers and mothers living in the United States, internal consistency levels were superior to 0.70 for the seven factors (9). On the other hand, the questionnaire was administered to 490 participants in a study conducted in Turkey; the reliability was tested by Cronbach's alpha coefficient, results showed higher internal consistency, Cronbach's alpha between 0.80 and 0.91 (14). Our study found a Cronbach's alpha coefficient for the seven factors between 0.67 to 0.86, and 0.75 for the complete questionnaire. Therefore, the CFQ could be useful to assess MCFP in Mexican mothers with similar characteristics to the participants in the present study.

The highest MCFP scores were found for perceived responsibility and monitoring, while the lowest scores were for concern about child weight and perceived child weight. These findings coincide with the research findings founded in a study conducted in Turkey (14).

As it was mentioned, among the seven factors of MCFP, perceived responsibility have the highest mean score, probably cultural implications attributed to maternal role may have influenced this result, given that, although almost half the mothers referred worked out of home, they decide how much food your child eat. Resulting in questioning about how this happens in daily life if the mother is working and another person is taking care of her child. Therefore, it is interesting to clarify this finding, to know details about how the mother decide how much food her child consumes if she is working.

The lowest MCFP scores were found for concern about child's weight and perceived child's weight. It should be noted; that the mothers are not concerned with their child's weight as long as their child is physically active (18), also the mothers tend to underestimate it (19). Other authors even indicate that the mothers are unable to perceive accurately her child's weight (20), and a study performed in Italy found an association between high prevalence levels of childhood obesity and inaccurate maternal perception of child's weight (21).

It is important to highlight that the perceived child's weight factor of CFQ assesses the parental perception of the child's weight across their lifetime, during the child's first year of life, between one and two years of age, between three and four years of age and so forth until the sixth year of elementary school. The mean score found in this study indicates the mother perceived her child's weight as right, however 36.01% of the children were overweight or obese, which was not recognized for the mothers. Therefore, a first step of the interventions to reduce or treat the child's excess weight is to help the mother to perceive accurately her child's weight.

This study demonstrated that perceived child weight was positively related (moderate and strong) with child's BMI and BFP. This finding is similar to result found in the study conducted in Italy that documented the relationship between inaccuracy MPCW and the high prevalence of childhood OW and OB(21).

On the other hand, given the increased prevalence of childhood obesity worldwide, including Mexico, is relevant to assess the body composition, especially the body fat mass, which is related to adverse health outcomes (22). However, given that we not found published studies about the BFP in Mexican children, further research about the body composition is recommended, including measurements of BFP and body fat distribution.

Finally, more than half of the mothers were pre-OB or OB, and the literature suggest that parents who are overweight, with problems controlling their food intake, or are concern about their child's risk for

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overweight, may adopt controlling child feeding practices in an attempt to prevent childhood OW. Unfortunately, research reveals this parental control attempts may promote the development of unhealthy eating styles and childhood OB(23).

Finally, the study limitations are that only mothers participated. Also, we not evaluated the relationship between variables such as education level, economic income, mother work status, or hours that mother works out the house with child's BMI and BFP.

In conclusion, the CFQ is an acceptable measure to assess MCFP in Mexican mothers. Also, mothers consider themselves responsible for feeding their children, but they do not have an accurate perception of her child's body weight, in addition, they trend to underestimate it; moreover an association was identified between the child's BMI and BFP, and perceived child's weight. The recommendation is to help the mother to recognize her child's body weight status before enrolment in interventions that target the child's excess body weight.

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Table 1: Internal Consistency of the Factors and the Child Feeding Questionnaire

Factor	Items	Cronbach's Alpha
Perceived Responsibility	1, 2, 3	0.78
Perceived Parent Weight	4, 5, 6, 7	0.67
Perceived Child Weight	8, 9, 10, 11, 12, 13	0.68
Concern About Child Weight	14, 15, 16	0.82
Restriction	17, 18, 19, 20, 21, 22, 23, 24	0.72
Pressure to Eat	25, 26, 27, 28	0.75
Monitoring	29, 30, 31	0.86
CFQ	1 - 31	0.75

Table 2: Characteristics of the Participants

Continuous Variables	Mean	Sd
Age		
Mother	34.18	6.79
Child	7.20	2.53
Bmi		
Mother	27.25	5.21
Child	17.79	3.60
Bfp		
Boy	25.90	9.92
Girl	27.20	8.79
Categorical Variables	N	%
Child Sex		
Boy	386	49.10
Girl	400	50.90
Mother Education		
No School	8	1.02
Elementary	78	9.92
Junior High School	190	24.17
High School	299	38.04
College	211	26.85
Mother Employed		
No	441	56.11
Yes	345	43.89
Maternal Weight Category		
Underweight	10	1.27
Healthy Weight	264	33.59
Overweight	289	36.77
Obesity	223	28.37
Child Weight Category		
Underweight	90	11.45
Healthy Weight	413	52.54
Overweight	172	21.89
Obesity	111	14.12

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Table 3: Descriptive Statistics of CFQ Factors

Variable	$\overline{X}$	SD	Value	
			Min	Max
Perceived Responsibility	84.35	16.99	16.67	100.00
Perceived Parent Weight	55.79	10.65	0.00	93.75
Perceived Child Weight	50.06	8.38	0.00	75.00
Concern About Child Weight	44.69	29.34	0.00	100.00
Restriction	60.86	20.26	3.13	100.00
Pressure to Eat	59.24	27.61	0.00	100.00
Monitoring	71.94	25.88	0.00	100.00
CFQ	61.00	10.44	28.54	86.31

Table 4: Association between the CFQ Factors and the Children's BMI and BFP

Factor	1	2	3	4	5	6	7	CFQ
BMI								
R_s	-.107	.175	.564	.250	.065	-.262	-.059	.051
P	.003	.001	.001	.001	.071	.001	.097	.156
BFP								
R_s	-.126	.180	.535	.242	.080	-.234	-.065	.053
P	.001	.001	.001	.001	.026	.001	.069	.139

1) Perceived responsibility, 2) Perceived parent weight, 3) Perceived child weight, 4) Concern about child weight, 5) Restriction, 6) Pressure to eat, 7) Monitoring BMI) Body mass index, BFP) Body fat percentage r_s) Spearman rank-order correlation coefficient, p) Level of significance.

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Evaluation of the Disease Surveillance System in Adjumani District Refugee Settlements, Uganda, April 2017

By Innocent Harbert Nkonwa, Emily Atuhaire, Denis Nixon Opio, Doreen Birungi, Benon Kwesiga, Dinah Nakiganda, Daniel Kadobera & Alex Riolexus Ario

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Abstract- *Background:* Adjumani District in Uganda has hosted refugees in camps since the onset of the South Sudan conflict in Dec 2013. Since then, Adjumani refugee settlements have experienced measles, cholera, and hepatitis E outbreaks. Health care, disease surveillance, and response for these refugees is carried out by both government health facilities and nongovernmental organizations (NGOs) using the Integrated Disease Surveillance and Response (IDSR) guidelines.

Methods: We evaluated attributes of the surveillance system using CDC MMWR 2001 guidelines for public health surveillance as a reference. Time liness was defined as proportion of reports received by the monthly due dates at the MOH. We interviewed District Health Team and health facility staff using a standardized questionnaire to determine their readiness to conduct IDSR, and used a checklist to ascertain the availability of surveillance tools.

Results: The surveillance system was adequate regarding stability, acceptability, and representativeness. NGO health facilities used HIS, which lacked some variables in the standard HMIS used by the MOH.

Keywords: *surveillance system evaluation, refugee setting, uganda.*

GJMR-F Classification: *NLMC Code: WA 420*

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Results: The surveillance system was adequate regarding stability, acceptability, and representativeness. NGO health facilities used HIS, which lacked some variables in the standard HMIS used by the MOH. We found poor timeliness [56%] and reporting rates [63%] across all diseases. The District Rapid Response Team [DRRT] and Epidemic Preparedness and Response Committee functioned only in confirmed outbreaks, and had no planning and review meetings.

Conclusions: The surveillance and response exist in Adjumani District but do not operate optimally. There was lack of harmonization between NGO surveillance activities and government health facility surveillance activities. We recommended harmonization of the HIS and HMIS reporting system in the district, and provision of appropriate recording and reporting tools by the District Health Officer.

Keywords: surveillance system evaluation, refugee setting, uganda.

I. Background

Populations affected by armed conflict, many in Africa and the Middle East, experience severe public health consequences as a result of population displacement, food scarcity, and the collapse of basic health services, giving rise to the term 'complex humanitarian emergencies' [1]. Countries in Africa such as South Sudan, Democratic Republic of Congo (DRC), Burundi, and Somalia have been heavily affected by conflict in recent years, leading to massive movement of refugees and internally-displaced persons [2]. Refugees and internally-displaced persons often experience elevated mortality rates during the period immediately following their migration, due to increased rates of diarrheal diseases, measles, acute respiratory infections, and malaria. High prevalence of acute malnutrition, especially amongst children, has compounded the problem further [3].

The conflict in South Sudan has resulted in massive displacement of its citizens to neighbouring countries. Uganda, South Sudan's neighbour to the south, has received over 640,000 refugees since the onset of the conflict in December 2013; this number has recently compounded due to renewed conflict and hostilities that began in July 2016. Presently, there are approximately 200,000 refugees, both Sudanese and Congolese, in Adjumani district in Uganda. The West Nile region of Uganda, which includes Adjumani district, experiences annual epidemics of cholera, meningococcal meningitis, plague, measles, and hepatitis E. These epidemics often have high case-fatality rates (CFRs) [2]. The hosting of Sudanese and Congolese refugees in this region has increased the risk for epidemics because of the poor living conditions in the camps and settlements.

The Adjumani Refugee Settlements were some of the first to receive and resettle refugees since the onset of the Sudanese conflict in December 2013. Currently, approximately half of Adjumani district's population of ~430,000 comprises refugees. This has increased the vulnerability of Adjumani district to both disease outbreaks and to seasonal peaks in malnutrition. Since the start of the emergency in South Sudan, refugees in the Adjumani settlements haveexperienced a measles outbreak in January 2014, cholera outbreaks in August 2015 and August 2016, and cases of hepatitis B. There is also high morbidity from childhood illnesses, particularly malaria, upper respiratory tract infections, and watery diarrhea,partially related to overcrowding in the camps[6]. These tend to peak during rainy seasons due to inadequate household hygiene and sanitation practices and poor or no vector control mechanisms.

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Integrated Disease Surveillance and Response (IDSR), developed by WHO/AFRO in 1998 and adopted by Uganda in 2000,is the national strategy for conducting and improving epidemiologic surveillance and response in Uganda, including in refugee settlements. In 2001, Uganda developed National IDSR Technical Guidelines, with emphases on epidemic-prone diseases, diseases targeted for elimination and eradication, diseases of public health importance [19]. Epidemic Prevention and Preparedness Response (EPPR) is part the Uganda National Minimum Health Care Package [1]. EPPR in Uganda is a mandate of Ministry of Health (MoH) as well as district governments. Epidemic-prone diseases in Uganda include cholera, bacillary dysentery, plague, meningococcal meningitis, viral hemorrhagic fevers (Ebola and Marburg), malaria, typhoid and hepatitis E [8]. Health care, disease surveillance, and response for refugees is carried out by both government health facilities and NGOs. In the data collection for IDSR, Ministry of health uses Health Management and Information system tools (HMIS) i.e. registers, forms, case investigation forms. The HMIS system ideally was supposed to replace the Health Information system (HIS) which is used by many NGO agencies.

Every surveillance system should be evaluated periodically with recommendations to improve its usefulness, quality, and effectiveness [8, 9]. We evaluated the public health surveillance system to determine Adjumani District's preparedness to implement IDSR [8].

II. Methods

Study Settings: Adjumani District has 17 resettlement camps for refugees, who are mainly from South Sudan and the DRC. The total refugee population for Adjumani District stoodat 209, 048 in 2017 [4]. The settlement areas are organised in clusters, blocks, and zones. A zone is the largest unit, which comprises 3 to 6 clusters. Clusters are smaller organisational units within the zones comprising groups of households. The households within the clusters are organised in blocks [4].

Study Design: We conducted a descriptive study to determine the readiness of Adjumani District Health Teams [DHTs] to conduct IDSR in April 2017. We evaluated the IDSR system serving the settlements using United States Centers for Disease Control [US CDC] guidelines for evaluation of public health surveillance systems. Eight health facilities [i.e. Adjumani hospital, Mungula HCIV, Lewa HCII, Pagirinya HCIII, Ayilo HCIII, Biira HCIII, Ayilo HCII, Pagirinya HCII] serving the five refugee settlements were considered for the evaluation. We assessed all health facilities for the recommended Ministry of Health staffing norms (i.e. for health center III, 2 clinical officers, 2 midwives, 3 nurses, 2 laboratory staffs,one health assistant, one records assistant; for health center II, one midwife, two nurses, one health assistant).

Data Collection: We conducted face-to-face interviews using a semi-structured questionnaire with the health facility [HF] in-charges and surveillance focal persons to collect information regarding the surveillance system attributes. We conducted focus group discussions with the District Epidemic Preparedness and Response Committee (DEPRC) and the District Rapid Response Team [DRRT] to obtain information on their functionality. We also held a consultative meeting with Village Health Teams (VHTs) and their focal persons to collect information on community surveillance.

Attributes of the Surveillance System Evaluated: We first developed a surveillance system description, including describing what the system was designed to accomplish, who the stakeholders were, system flow, data use, case definitions, detection algorithms, privacy/confidentiality, and communication of data. Next, we assessed multiple attributes, including those below, and made conclusions and recommendations for use and improvement of the syndromic surveillance system.

Usefulness: ways the system had demonstrated value relevant to public health Acceptability: stakeholders' willingness to contribute to and use the system. Generalizability: how readily the system could be duplicated in another location Stability: the reliability (i.e., the ability to collect, manage, and provide data properly without failure) and consistent availability (the ability to be operational when needed) of the public health surveillance system. Flexibility: How adaptable the system was to changing needs and risk thresholds. Sensitivity: the proportion of cases and outbreaks detected by the system that were true cases and outbreaks, and proportion of alarms triggered by the system that are true alarms (true positives).Timeliness: reporting was assessed as timely if the reports were within the Ministry of Health recommended timelines and late if otherwise. Representativeness: how well the system reflected the population of interest. Completeness: proportion of data that were present for each record. Reliability: measure of how well the data captured were consistently across the system and over time.

Ethical Consideration: The Ministry of Health of Uganda through the office of the Director General Health Services gave the approval to conduct this investigation. Additionally, the office of the Associate Director for Science, US Centers for Disease Control and Prevention, Uganda, determined that this investigation was not human subjects' research because the primary purpose was to identify, characterise, and control disease in response to a perceived immediate public

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health threat. Permission was also received from the Adjumani District Health Officer. The qualitative interviews were only conducted after written informed consent was given to the participant.

III. Results

a) Description of the Surveillance System

Adjumani District government health facilities currently use the IDSR system to report epidemic-prone diseases [11]. Due to unavailability of reliable power in many peripheral facilities, the paper-based system is used in these facilities, while the electronic system is used from the district office upwards. In brief, healthcare workers at government health facilities identify suspected cases of epidemic-prone diseases and fill in standardized paper HMIS paper case report forms for the appropriate disease. The forms are dispatched manually to the District Health Office, where the District Biostatistician enters and analyzes the data inDHIS2 (District Health Information Software2) and then submits to MoH. The MoH summarizes these data on a monthly and quarterly basis.

On a weekly basis, health facilities also use a system called Mtrac (Mobile tracking of Health Services), which involves the use of toll-free cellphones to relay information on epidemic-prone diseases as well as medicine stock balances to the district health office, where the data are cleaned, validated, and approved before submission to MoH. These data are integrated into the monthly report from the District to the MoH. The ministry gives feedback to through assessment of the performance indicators as per the sent reports.

Of the eight sites supporting the refugee camps in Adjumani District, four are supported by the Ugandan government and four by NGO implementing partners. The implementing partner-supported sites have another, parallel system of reporting, whereby the facilities use a largely paper-based system with HIS (Health Information System, different from HMIS) forms to collect information. These data are relayed from the facilities to the NGO implementing partners, which also have a biostatistician to aggregate and analyze data, and relay it back to the district.

b) Information Flow

At all the health facilities visited respondents were conversant with the flow of information, however; the reporting system was adhered to by the government-supported facilities only. Reporting tools used by the NGO-run facilities were different from the tools used by the government facilities (HIS vs HMIS), and NGO-run facilities were not reporting to the Uganda MoH system. Most of the reporting was to United Nations High Commissioner for Refugees (UNHCR). All the health workers interviewed reported lack of feedback from their superiors about the submitted reports.

The District Epidemic Prevention Preparedness and Response Committees (DEPPRC) or disaster committees were present in Adjumani district, though found to be only functional during times of outbreaks and disasters. Ideally, these committees are supposed to sit on a quarterly basis to review their epidemic preparedness plans.

Of the 8 health facilities visited, 5 (63%) adhered poorly to the IDSR-recommended systems for surveillance. No health facility displayed information on priority diseases. All health facilities were ill-prepared to handle emerging epidemics. There were no supplies appropriate for an emerging epidemic, such as personal protective equipment or disinfectants, and none of the facilities could estimate supplies for emergencies. Feedback mechanisms on the submitted reports and samples sent to the national laboratories were found to be very poor from the district and national level; many of the health facilities serving refugee populations reported having sent suspected laboratory samples to the district and MoH without receiving feedback on results.

c) Laboratory Infrastructure

We found that the laboratory infrastructures at the periphery of the district serving the camps compromised regular and outbreak surveillance functions due to inability to diagnose epidemic-prone diseases. Suspected cholera and measles samples had to be transported to the district, then to the regional referral hospital for diagnosis, while samples from patients with suspected rubella and viral hemorrhagic fevers needed to be transported to the Uganda Virus Research institute, far from the site. There were no specimen/sample collecting bottles in any laboratories; laboratories were improvising with used intravenous drug bottles. Many HCII facilities were the first contact for diagnostics in refugee settlement areas, and none of them had a laboratory facility (as per the MoH policy). Only the district hospital could confirm some of the priority diseases. Health Centre IIIs and IVs had laboratories, although their capacities were limited. Sample collection for HIV treatment monitoring (viral load, CD4, Renal and Liver function tests) and transportation was good and this was complemented by the national sample transportation system (hub system).

d) Attributes of the IDSR system for Adjumani District

Surveillance System Resource Requirements: The surveillance system had no separate budgetary allocation for its operation. Prioritization of the surveillance activities in the district and facility work plans was lacking in all facilities. All the health facilities had an accessible means of transport to deliver specimens and suspected patients to the district hospital. However, there were no specimen/ sample collection containers in any facilities except Adjumani Hospital.

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Usefulness of the Surveillance System: The surveillance system in Adjumani was found to be sub-optimally functional in terms of data use. Data were used to make decisions only during epidemics. These data were not usedto make realistic estimations of resource requirements for prevention and containment of an epidemic or for program planning, nor to calculate baseline levels of disease.

Human Resource Capacity: All health facilities selected had designated surveillance and HMIS staff. Non-governmental organization-supported facilities were overstaffed, according to MoH staffing norms.

Timeliness: The reporting rates for most health facilities were poor with government facilities (i.e., Adjumani hospital, Mungula HCIV, Biira HCIII, Lewa HCII) having late reporting and most NGO facilities were not reporting at all (Table 4).

Simplicity: The system was found to be complex in structure as evidenced by special or follow-up laboratory tests to confirm the case; investigation of the case, including telephone contact or a home visit by public health personnel to collect detailed information; multiple levels of reporting (e.g., with the National Notifiable Diseases Surveillance System, case reports might start with the health-care provider who makes the diagnosis and pass through county and state health departments before going to CDC [29]); and integration of related systems whereby special training is required to collect and/or interpret data. Many health workers were not even aware of the standard case definitions. Data flow wasn't systematic (i.e. from health center to health sub district then to district as recommended by MoH). The case investigation forms were not readily available at the health facilities, and one had to consult the DHOs office in case of a suspected epidemic-prone condition for verification by the district surveillance focal point person. This was more evident among the non-government health facilities; health workers from some of these facilities had never seen case investigation forms. There were multiple levels of reporting of suspected events, with the NGO-supported sites having the HIS system as opposed to the HMIS recommended by the Uganda MoH, and reporting to their agencies before reporting to MoH.

Flexibility: Flexibility was evaluated retrospectively by observing how a system had responded to a new demand. There were revised case definitions, additional data sources, new information technology, and challenges in funding. The system had failed to integrate the HIS with the recommended HMIS, which offered immense challenges to the service providers, primarily in the partner-supported sites when some information required by HMIS was not captured by the HIS tools. All NGOs are supposed to report through the MoH structure; however, the HIS tools didn't capture some of the required MoH variables.

Acceptability: The NGO-supported health facilities had a parallel structure for reporting through the HIS. This allowed them to bypass the MoH reporting system and report to their donors. Data flow wasn't through the MoH. Most of these facilities did not report through the HMIS system, and those that did were either late or incomplete.

Sensitivity: The system was found to be sensitive because it was able to detect epidemic prone diseases or other health-related events that were occurring in the population under surveillance. Since the start of the emergency in South Sudan, refugees in the Adjumani settlements have experienced a measles outbreak in January 2014, cholera outbreaks in August 2015 and August 2016, and cases of hepatitis B. The system was able to detect and report all these outbreaks.

Data Quality: The quality of data was poor. Specifically, there were many missing variables leading to incomplete data. The registers in some of the NGO health facilities were lacking standard reporting tools and were using different tools for data collection with most required variables not captured.

Stability: The system was found to be unstable primarily because most health facilities were using a manual system to generate and store data (i.e., paper-based). Tracing reports in most health facilities was difficult. There were no funds for surveillance activities in all the health facilities, with funds only being availed after outbreaks are confirmed.

Representativeness and Completeness: Four out of the eight health facilities assessed consistently reported in their monthly and weekly reports on the reportable diseases. In four health facilities, weekly reports were missing.

Data Analysis: Data were neither analysed at the health facility nor the district level.

IV. Discussion

The surveillance system in the refugee settlements of Adjumani District faced many challenges, which likely compromised its effectiveness. We found the surveillance system to be lacking in all the attributes assessed except sensitivity, as there was evidence that it was achieving one of the key surveillance objectives of detection and prevention of epidemics. Evaluation of the surveillance system was designed to help policymakers in the given country to set priorities for future planning, resource allocation, and future interventions to help prevent disease [12, 13]; however, the challenges faced by the system in its current state will make that difficult.

Although DEPPR and DRRT structures existed in the district, they only met during outbreaks and times of disaster. Similar findings were found in a study in West Nile where many district committees didn't convene meetings regularly [14]. The reasons for the

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noncompliance in our study was due to the underfunding by the district to carry out surveillance activities and lack of prioritisation.

Most health facilities were not using the IDSR tools, and reporting rates for Adjumani were below the national target of 80%. Non-governmental health facilities mainly serving the refugee settlements did not report to the MoH [11]. This could bepartially explained by the fact that there is a parallel system of reporting for United Nations High Commission for Refugees (UNHCR)/Medical Teams International (MTI)-supported units with the health care workers using HIS (as opposed to the HMIS reporting system from MoH), and that the facilities did not want to double-report [15]. However, NGO-supported health facilities' failure to reportaffected the general reporting rates for the district and surveillance as a whole, as it compromised the ability to detect outbreaks in the district. The NGO-supported health facilities also lacked the standard MoH tools such as the case investigation tools and registers.

Although an electronic system was implemented in 2012 the reporting systems were primarily paper-based,with only a few facilities having access to the electronic system. This was due to irregular power supply in the remote settlements. This failure to be able to use an electronic system affected reporting timeliness, and, in the long run, timely detection of outbreaks. Most health facilities serving the resettlement areas were overstaffed with highly qualified staffs according to the MoH staffing norms. However, these additional staff could be useful in assisting with surveillance.

Limitations: We were not allowed access to source data to evaluate the system through audits.

V. Conclusions

Generally, the structures for epidemic preparedness and prevention exist in Adjumani District but are operating sub-optimally. There was lack of harmony in the operations of NGO agencies and government health facilities in the performance of the surveillance function.

VI. Recommendations

We recommended harmonization of the HIS and HMIS reporting system in the district, and provision of appropriate recording and reporting tools by the District Health Officer. There is need to avail the case investigation tools, case definitions booklets and charts, standard tool to both governmental and non-governmental facilities. The DHO's office should have a contingency plan in case of epidemics. Supportive supervision of health facilities should be stepped up to improve on upward reporting of HMIS data. The district laboratory should be supported to procure and stock transport media for proper collection and transport of clinical specimens during particular disease outbreaks.

Public Health Actions: Following the evaluation, we conducted IDSR training for 25 health workers serving the settlement area as a way of addressing some of the identified gaps. In collaboration with Adjumani DHT and Action Against Hunger (ACF), we developed the District Epidemic Preparedness and Response Plan.

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Competing Interest

The authors declare that no competing interests exist.

Authors' Contribution

Innocent Herbert Nkonwa, Emily Atuhaire, Benon Kwesiga, Dinah Nakiganda, Daniel Kadobera, Alex Riolexus Ario, Uganda Public Health Fellowship Program, Kampala, Uganda. Ministry of Health, Kampala, Uganda. These authors contributed equally to this work.

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Table 1: Epidemic Preparedness Measures in Adjumani District, April 2017

Measure of Preparedness	Results
Presence of District EPPR or Disaster Committee	Yes, Headed by District Health Officer
Functionality of Depprcs	No, Only Met During Outbreaks
Duration (in Months) The Committee Last Met	14, When they Last had an Outbreak
Presence of Comprehensive EPPR Plan(S)	No
Presence of Drrts	Yes and Functional
Presence of Log of Suspected Rumors	Yes, District Surveillance Focal Person Takes Lead
Availability of Notification Forms	Yes, at District
Availability of Case Definition Booklets	Yes, at District
Availability of Line Listing Forms	Yes, at District
Availability of Case Management Protocols	Yes
Buffer Stock of Essential Medicines and Health Supplies	No
Capacity of Lower Level Facilities to Diagnose Epidemic Prone Diseases	No
Presence of Laboratory Designated for Case Confirmation	Yes, at Arua Regional Referral Hospital, Adjumani Hospital and Central Public Health Laboratory
Occurrence of EPPR Trainings for Health Workers in the 1 Year Preceding this Study	Yes, Preparing for Previous Outbreak
Number of EPPR Trainings Held if any	1
Formation of Lower Local Government (S/C) EPPR Committees	No
Training of Members of Lower Local Government (S/C) EPPRC in Last 1 Year	Yes
Community Mobilization & Sensitization Activities Implemented	Yes, Mainly By Implementing Partners

Table 2: Capacity of Health Facilities for Analysis, Interpretation, Confirmation, and Investigation of Reported Cases of Epidemic Prone Diseases in Adjumani Refugee Settlements, April 2017

Surveillance Function	Indicator	Percentage
Data Analysis and Interpretation	Drawing of Graphs on Priority Diseases	50
	Display Information on Priority Diseases	0.0
Investigation and Confirmation of Reported Cases	Reported a Suspected Epidemic Prone Disease in the Last 8 Weeks	17
	Immediate Reporting of the Epidemic Prone Diseases to the District	17
	Laboratory Results Received from Reference Laboratories	100
	Availability of Appropriate Supplies for Specimen Collection during Urgent Situations	0.0
Response	Availability of Appropriate Supplies for Responding to Confirmed Outbreak	0.0
	Health Facility has Surveillance Focal Person	50
	At least One Staff at Health Facility Trained in IDSR	50
Feedback	Health Facility Provides Feedback to the Community through VHTs	33
	Health Facility Receives Feedback from District	00
	Receives Latest Bulletin from Central or Sub-National Level	0.0
Evaluate and Improve System	Health Facility sent the Last 3 Monthly Reports to the District	17
	Weekly Reports sent on Time	36
Epidemic Preparedness	Knows how to Estimate Supplies in Emergency Situations	0.0
	District Leaders Conducted Supervisory Visits	33

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Table 3: Staffing Levels of Health facilities serving 5 Refugee settlements in Adjumani District, April 2017

Human Resource Assessment Areas	Pagirinya HCIII	Pagirinya HC II	Ayilo HC III	Ayilo HC II	Lewa HC II	Bira HC III	Mungula HC IV
Nurses	8	5	10	4	2	8	11
Midwives	4	1	4	3	2	5	5
Clinical Officers	3	2	4	2	0	2	4
Doctors	0	0	1	0	0	0	2
Laboratory Staff	2	2	3	1	0	2	3
Environmental Health	1	0	1	0	0	1	0
Others	3	10	7	19	1	15	4

Table 4: Timeliness for the Facilities Serving the Adjumani Refugee Settlements Sampled for the Dirst 12 Epi Weeks 2017

Name of Health Facilities	Timeliness	Completeness
Adjumani Hospital	62	100
Mungula HCIV	54	69
Bira HCIII	85	100
Lewa HCII	62	100
Ayilo HCII	0	0
Ayilo HCIII	31	54
Pagirinya HCII	0	0

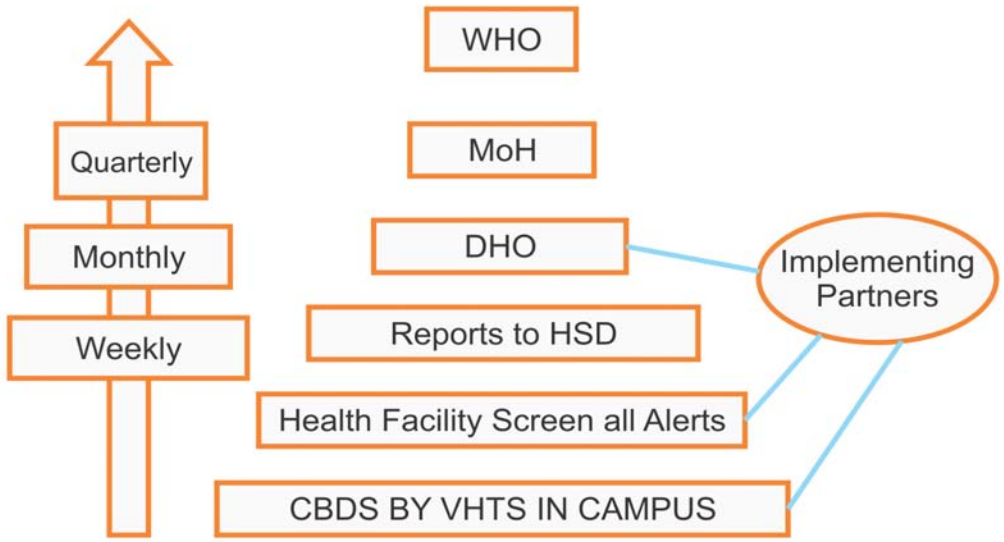

Fig. 1: Structure and organization of the Disease surveillance system in Adjumani District, April 2017

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Social Support, Stressful Life Events, Medication - Taking Self - Efficacy, Psychotic Symptoms on Social Dysfunction: Role of Mediating Effects

By Imkome E., Yunibhand J., Chaiyawat W. & Nouanthong P.
Thammasat University

Abstract- *Background:* Understanding the role of mediating effects of psychotic symptoms and medication-taking self-efficacy on Social dysfunction could help identifying persons at the risk of progression to schizophrenia with methamphetamine misuse and guide early integrated relapse intervention.

Objectives: To test a hypothetical model of psychotic symptoms in persons with schizophrenia and misusing methamphetamines and to test the mediating effects of psychotic symptoms and medication-taking self-efficacy on Social dysfunction.

Methods: In a cross sectional-study, 313 participants from 9 settings were enrolled. A set of five questionnaires were applied, including of the Demographic Data Questionnaire, the Brief Psychiatric Rating Scale, the Self-efficacy for Appropriate Medication Use Scale, the Stressful Life Events Questionnaire, and the Social Dysfunctioning Scale, paralleled with social support questionnaire. Path analysis was used to test the model and hypothesis to predict the mediating effects.

Keywords: *social support, medication taking self-efficacy, social support, social dysfunction, path analysis, psychotic symptoms, schizophrenia, methamphetamine misuse.*

GJMR-F Classification: *NLMC Code: WL 103*

Strictly as per the compliance and regulations of:

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Social Support, Stressful Life Events, Medication-Taking Self-Efficacy, Psychotic Symptoms on Social Dysfunction: Role of Mediating Effects

Imkome E. [α], Yunibhand J. [σ], Chaiyawat W. [ρ] & Nouanthong P. [ω]

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Results: The model indicated a good fit of the data ($\chi 2 = 114$, df = 92, p-value = 0.057, GFI = 0.96, AGFI = 0.92, CFI = 1.00, RMSEA = 0.028. The path analysis showed that social support, medication-taking self-,and psychotic symptoms had a positive direct effects on social dysfunction in schizophrenia and misused methamphetamines persons. The explanatory variables accounted for 26% of the variance in explaining social dysfunction. Medication self-efficacy had direct effect on psychotic symptoms. Social support had direct effect on medication use self-efficacy. Psychotic symptoms had the largest and a significant direct impact on social dysfunction. Social dysfunction was inducible from the stressful life event, but it could be mediated by efficacy of the treatment.

Conclusions: Psychotic symptoms was the most important predictor for persons with schizophrenia and misused of methamphetamine. The psychotic symptoms are playing a significant role on social dysfunction. Early symptoms detection can guide the nursing intervention, integrated treatment plans, and the supportive social program to reduce patient's social dysfunction and enhance their quality of life.

Keywords: social support, medication taking self-efficacy, social support, social dysfunction, path analysis. psychotic symptoms, schizophrenia, methamphetamine misuse.

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I. Introduction

The global burden of comorbidity attributable to illicit drug uses. Of those 247 million illicit substances users, at least one in 2014, 29 million suffers from drug used disorders (1). People who suffer from drug used disorders or people with drug use disorders were a subset of population who use drugs and need treatment, health and social care, and rehabilitation. Methamphetamine use mimic schizophrenia and it is estimated that 30% within 8 years of those users will be diagnosed with a stimulant-induced psychosis and will be re-diagnosed with schizophrenia that psychotic symptoms was play a vital role. Additionally, methamphetamine use is associated with poorer social dysfunctioning and prognosis in persons with primary psychotic disorders, such as schizophrenia spectrum disorder (2-3).With this regards, it is a need to discover what factors related to psychotic relapse among schizophrenic Persons with methamphetamines misused (4-6). Early detection and preventive intervention can be provided to reduce the subsequent risk of transition to schizophrenia and relapsing of schizophrenia in long terms. One direction of identifying which cases are likely to progress to schizophrenia is to examine their symptom patterns, factors influencing, and mediating effects of factors related to psychotic symptoms. Particular positive symptoms such as bizarre thinking have been shown to predict psychosis onset among prodromal / high-risk individuals (6-8).

This type of positive symptoms experienced may be an indicative individual as persons with methamphetamine are more likely at risk of progressing to schizophrenia. Although numerous of empirical studies indicated that, the prevalence of psychotic symptoms in MAP, primarily persecutory delusions and hallucinations (usually visual and auditory), the structure or typologies of psychotic symptoms in MAP has yet to be undertaken. Moreover, 12 million injected drugs users, they are likely high risk of infection: HIV (14%) and

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HCV (52%) (7). In addition, global consequences of SUDs are far-reaching to higher rates of comorbidity such as hepatitis and tuberculosis infections, lost productivity, injuries and deaths from automobile and other accidents, as well as deaths from overdose drug used, suicides, and violence (6, 10).

Psychotic relapse prevention for persons with schizophrenia and misusing methamphetamine is becoming an urgent public health needed. However, there are some concerning conflicting ideas, which variables are most important and whether these variables are "direct or indirect" factors, impact on psychotic symptoms (4, 11). Specific predicting factor for this hypothetical model could not easily be extracted from the result of empirical research. This study is, therefore, exploratory.

There were numbers of evidence based studies to examine antecedents of psychotic symptoms (4, 7, 12, 13), but little is known about relationships in these factors, for example, social support, stressful life events, medication used self-efficacy, and what psychotic symptoms play as the mediating role effected on social dysfunction that deteriorated on the severity of psychotic symptoms. Design suitable intervention program and extensively program used as psychiatric and mental health nursing is the important issue to prevent relapse and being a positive influences on nursing outcomes and multidisciplinary treatment teams outcomes.

Considering varies variables, we attempted to identify the associated factors with psychotic symptoms among schizophrenia and misusing methamphetamines users by creating a path model. Both direct and indirect factors were included in the study. The initial hypotheses of the study included: (a) whether psychotic symptoms would be the most powerful direct predictor social dysfunction of in persons with schizophrenia, misusing methamphetamines: (b) could psychotic symptoms and medication-taking self-efficacy mediate social dysfunction.

The results of this exploratory study could generate insight understanding in the existence of different diurnal fluctuations or deviant within-subject relationships between medications used self-efficacy and psychotic symptoms. These results may also provide further knowledge on the within-subject relationship between social dysfunction and stressful life events versus social support of the stress and physiological systems.

II. Purpose

To test a hypothetical model of psychotic symptoms in persons with schizophrenia and misusing methamphetamines and to test the mediating effects of psychotic symptoms and medication-taking self-efficacy on Social dysfunction.

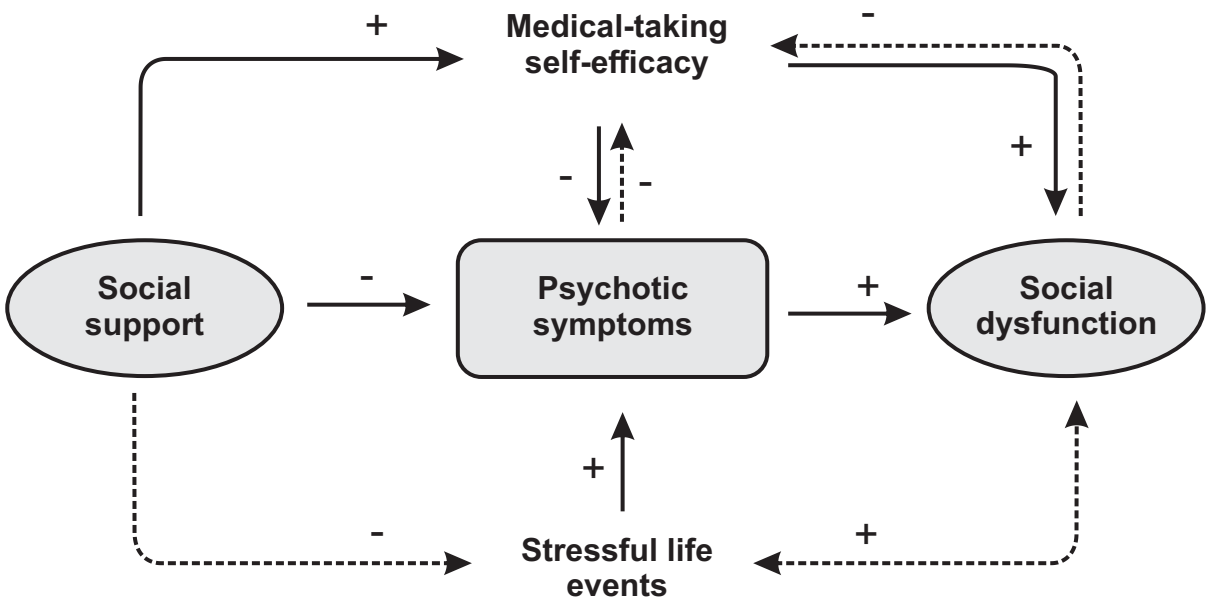

Diagram 1: Association of Medication, Social Events, Social Support and Social Dysfunction

III. Methods

The cross-sectional study was conducted during April to May 2015 at the psychiatric hospital and Institute on Drug Abuse Treatment, Thailand.The Ethics Review Committee for Research Involving Human Research Participants, Health Science Group, Chulalongkorn University (COA approved this study.No. 053/2558). The risk and benefits of participation were explained to the participants. Written consent forms were obtained directly from participants before data collection. Participation was voluntary, and anonymity. Confidentiality of participation were guaranteed. Data collection were based on questionnaires.

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a) Measures:

1. The Brief Psychiatric Rating Scale (BPRS) (15) use to measure psychiatric symptoms, a semi-structured interview with an 18-item rating scale based on patient observations and verbal reports. The total scale score ranges from 18- to 126, from "not present" to "extremely severe." The BPRS exhibited reliability = 0.98 and intra class correlation coefficient = 0.88 (13).
2. The Self-Efficacy for Appropriate Medication Use Scale(16) with 13 items was in two dimensions: the first was self-efficacy for taking medications under difficult circumstances, and the second self-efficacy for continuing to take medications when circumstances of taking medication are uncertain. The Likert scale ranged from not confident to very confident. Scores ranged from 13 to 39. The SEAM showed Cronbach's alpha = 0.91, item-total correlations ranging from--0.07 to 0.62, and test retest = 0.97.
3. Thai Stressful Life Events Rating Scale (TSLERS) (17). The TSLERS is a self-report with two constructs, including self-perceived frequency and intensity of stressful life events. The TSLEQ consisted of 46 items on a 6-point Likert scale, ranging from "never" to "very severe." The 11 domains covered home life, financial problems, social relations, personal conflicts, job conflicts, educational concerns, job security, loss and separation, sexual life, daily life, and health concerns. In the validity of the barriers using seven content experts, the CVI was 1.0, Cronbach's alpha = 0.97, item-total correlations ranged from 0.27 to 0.92, and test retest = 1.00.
4. Social Support Questionnaire (SSQ) (18) consisted of two parts designed to measure informational, emotional, and tangible support. The questionnaire consisted of seven items on three resources of support: one for information support, four for emotional support, and two for tangible support. SSQ was rated on the Likert scale ranging from "not at all" to "a great deal." Scores for three types of support from all sources were added to produce a total social support score. SSQ showed Cronbach's alpha = 0.93, item-total correlations ranged from 0.38 to 0.67, and test retest = 0.95.
5. The Thai Social Dysfunctioning Rating Scale (TSDRS) (19). The SOFS is an observer rating scale comprised of two main components:
   i. The ability to look after oneself and maintain daily activities.
   ii. The instrumental and social skills to manage oneself and live in the community.

Each item is rated on a 5-point Likert scale ranging from "no impairment" to "extreme impairment." The measurement showed CVI = 1.00, construct reliability = 0.99, Cronbach's alpha = 0.93, item-total correlations ranging from 0.30 to 0.70, and test retest = 0.96.

IV. Statistical Analysis

Path analysis was developed: it was used to assess and to compare the fit of the models as three steps below:

1. Confirmatory factor analysis was conducted by estimated using maximum likelihood (ML) with two latent variables (psychotic symptoms and medication-taking self-efficacy) to test the modelfit and constructing the full path model then. The model fit was evaluated using Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), and Standardized Root Mean Square Residual (SRMR) because the $\chi 2$ statistic is sensitive to a large sample size.
2. An SEM path analysis estimated using ML that identified latent and observed variables while covarying for age and gender was conducted. Two latent variables using the psychotic symptoms and medication-taking self-efficacy were defined as indicators by fixing the loading of thefirst parcel in each factor to 1. The social support and stressful life events subscale scores were included as observed variables. Pathways from social support and stressful life events to the medication-taking self-efficacy and psychotic symptoms to social dysfunction were examined in a cross-sectional model.
3. SEM moderation analyses estimated with ML was conducted. Variables as described above were defined. In present model, the medication-taking self-efficacy and psychotic symptoms was considered as a moderator in the relationship between social support and stressful life events on social dysfunction.

V. Results

Persons who met the inclusion criteria (n = 313) were enrolled in the study. All of them had have experiences of psychotic symptoms. Predominately subjects were male (87.9%), from high-school (27.8), being single (66.8%) and employment (28.4%). The mean age was 25 years old. From the first time of diagnosis of schizophrenia, a number of seeking care admitted, duration of having psychiatric illness were 2-10 years, 2-5 times, and 1-5 years, respectively. No physical illness, but most of them had psychiatric illness (70%). Regarding patient's medical history, nearly half of them (47.0%) had duration of psychiatric illness from 1-5 years. Over two-thirds of them were treated with antipsychotic drugs (73.2%) and group therapy (87.2%). Nearly half participants consumed 2 to 5 tablets of

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methamphetamine daily (48.2%). The primary route of methamphetamine usage was smoking (91.1%), and more than half of the Persons (62.3%) have concurrently smoked cigarettes. They were under antipsychotic drugs (73%), with antipsychotic drug (23%) and experienced group therapy (87%) (Table 1).

Table 1: Demographic Characteristics of Schizophrenic Patient and Misusing Methamphetamines (n = 313)

Characteristics	Number	Percentage
Age (Years)		
19 – 30	143	46.3
31 – 40	126	40.3
41 – 50	38	12.1
51 – 60	4	1.3
Gender		
Male	275	87.9
Female	38	12.1
Marital Status		
Single	209	66.8
Marriage	54	17.3
Widowed	10	3.2
Divorced	15	4.8
Separated	25	8.0
Education		
None	14	4.5
Primary / Elementary Education	12	3.8
Secondary Education	73	23.3
High School	87	27.8
Diploma / Certificate	86	27.5
Bachelor's Degree or Higher	20	6.4
Occupation		
Government Official	15	4.8
Employee	89	28.4
Business Person	64	20.4
Agriculturist	71	22.7
Unemployed	73	23.3
Housewife	1	0.3
Number of Admitted		
2 - 5 Times	261	83.4
6 - 10 Times	39	12.5
> 10 Times	13	4.2
Duration of having Psychiatric Illness		
< 1 Years	80	25.6
1 - 5 Years	147	47.0
6 - 10 Years	33	10.5
11 - 15 Years	33	10.5
15 - 20 Years	15	4.8
> 20 Years	5	1.6
Physical Illness		
None	276	88.3
Gastritis	10	3.3
Hypertension	5	1.7
Asthma	3	1.0
HIV	2	0.6
Thalassemia	2	0.6
Migraine	1	0.3
Renal Failure	1	0.3
Hyperthyroid	1	0.3
Hypercholesterol	1	0.3
Gastritis and Asthma	1	0.3
Gastritis and Hypertension	4	1.2
Hypertension and Renal Failure	2	0.6

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Diabetes Mellitus, Hypercholesterol, and Hypertension	2	0.6
Smoking Status		
No	2	0.6
Ex-Smoking	116	37.1
Smoking	195	62.3
Treatment		
Pharmacotherapy		
None	3	1.0
Antipsychotic Drugs	229	73.2
Antidepressant	1	0.3
Anxiolytic Drugs		
Antipsychotic Drug and Antidepressant	72	23.0
Antipsychotic Drug, Antidepressant, and Bupropion HCl	4	1.3
Antipsychotic Drugs and Propylthiouracil	1	0.3
Antipsychotic Drugs and Antipsychotic Drugs and	1	0.3
Antipsychotic Drugs and AZT	2	0.6
Group Therapy	273	87.2
ECT	11	3.5

Major social support was family. There was the relationship of patient's stressful life events associated such as job conflicts, sexual life, education concerns, social relations, daily life, and personal conflicts, respectively (Table 2)

Table 2: The Relationship of Observed Variables and Attributable (Loading Factors, Standard Error, T-Test, Lambda-X, and Square Multiple Correlation)

Observed Variables	Loading	SE	T	λ	R2
Social Support					
Family	6.09	0.47	12.84	0.78	0.61
Healthcare Team	5.20	0.43	12.13	0.69	0.48
Neighbors and Friend	3.51	0.48	7.27	0.42	0.18
Stressful Life Event					
Home Life	5.23	0.48	10.80	0.56	0.32
Financial Problems	5.15	0.34	15.04	0.74	0.55
Social Relations	5.15	0.28	18.64	0.86	0.74
Personal Conflicts	5.43	0.35	15.55	0.79	0.62
Job Conflicts	4.69	0.25	18.77	0.87	0.76
Educational Concerns	4.74	0.25	19.06	0.87	0.75
Job Security	5.61	0.33	16.78	0.80	0.64
Loss And Separation	5.08	0.29	17.79	0.83	0.69
Sexual Life	4.50	0.24	18.81	0.87	0.76
Daily Life	4.62	0.25	18.70	0.86	0.73
Health Concerns	2.25	0.14	16.49	0.79	0.62
Psychotic Symptoms					
Positive Psychotic Symptoms	0.22	-	-	0.63	0.40
Negative Psychotic Symptoms	0.16	0.05	3.37	0.47	0.22
Affective Psychotic Symptoms	0.09	0.06	1.47	0.12	0.01

Social support had significant direct effect from medication-taking self-efficacy, but indirect effects from psychotic symptoms and social dysfunction. Persons had significant stressful life event associated with social dysfunction. For self-efficacy in taking medication, psychotic symptoms and social dysfunction were associated (Table 3).

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Table 3: Total Effect (TE) Direct Effect (DE) and Indirect Effect (IE) of Factors Influencing Social Dysfunction

Independent Variable	Dependent Variables								
	Medication use Self-Efficacy			Psychotic Symptoms			Social Dysfunction		
	DI	IE	TE	DI	IE	TE	DI	IE	TE
Social Support	2.33**	-	2.33**	-	-0.09*	-0.09*		-0.56*	-0.56*
	(0.56)		(0.56)		(0.04)	(0.04)		(0.23)	(0.23)
	0.36		0.36		-0.09	-0.09		-0.06	-0.06
Stressful Life Event	0.02	-	0.02	-	0.00	0.00	2.72**	-0.01	2.71**
	(0.43)		(0.43)		(0.02)	(0.02)	(0.52)	(0.10)	(0.53)
	0.00		0.00		0.00	0.00	0.29	0.00	0.29
Medication Self-Efficacy				-0.04**	-	-0.04**	-	-0.24**	-0.24**
				(0.01)		(0.01)		(0.07)	(0.07)
				-0.25		-0.25		-0.17	-0.17
Psychotic Symptoms							6.21*	-	6.21*
							(2.39)		(2.39)
							0.67		0.67
R^2	0.13			0.07			0.10		
$\chi 2$ = 114, df = 92, p-value = 0.055, GFI = 0.96, AGFI = 0.92, CFI = 1.00 , RMSEA = 0.028									

Note * $p < 0.05$, ** $p < 0.01$

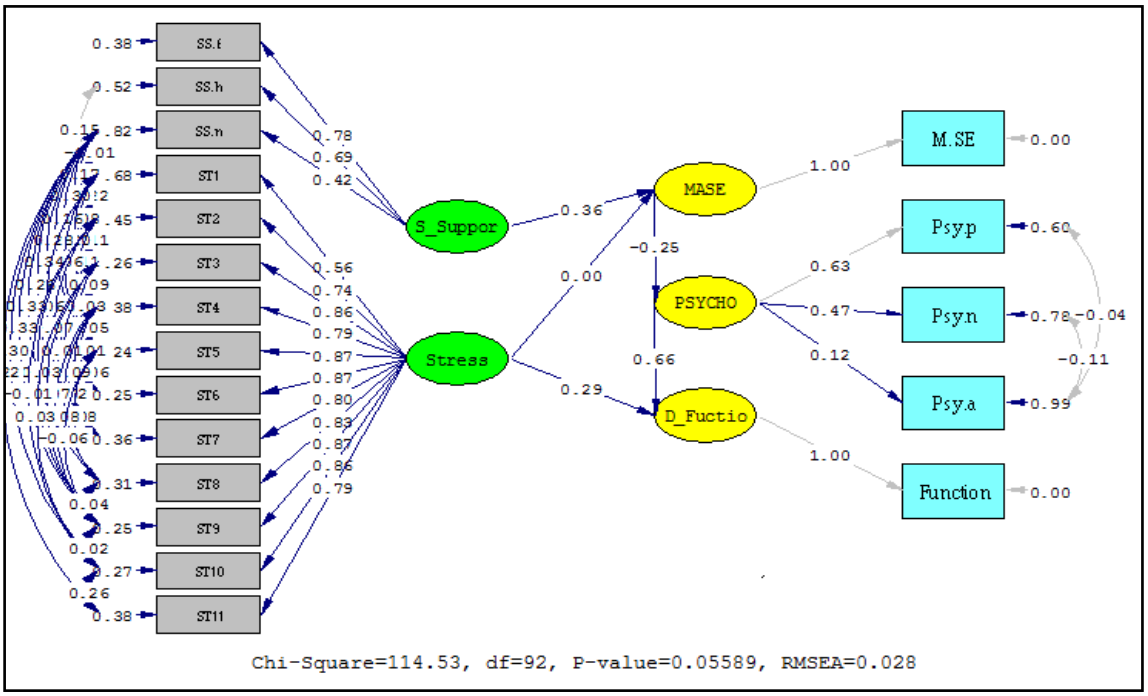

Fig. 1: A Path Analysis of Psychotic Symptoms among Schizophrenic Persons with Misusing Methamphetamines

A path analysis of psychotic symptoms among schizophrenic persons was developed and verified. The model indicated a good fit of the data (X2 = 114, df = 92, p-value = 0.056, GFI = 0.96, AGFI = 0.92, CFI= 1.00, RMSEA = 0.028. We found that psychotic symptoms had positive direct effects on problem focused coping, expressed emotion, social support, and medication-taking self-efficacy. There was 26% of the variance to explain the psychotic symptoms. Social support, especially, family had direct effect on medication-taking self-efficacy. Medication self-efficacy had direct effect on psychotic symptoms. The association of the treatment efficacy mediated on social dysfunction. Stressful life event was also attributable direct effect on social dysfunction (as showed in diagram 1)

VI. Discussion

The depicted finding indicated that social support had direct effect on increasing of medication-taking self-efficacy. In addition, medication-taking self-efficacy had direct associated effect on psychotic

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symptoms with the decrease in psychotic symptoms. Both associations are mediated on social dysfunction.

Stressful life events have possibility of indirect effect on social dysfunction through medication-taking self-efficacy and psychotic symptoms. It could explain that the participants encountered with the severe stress in their life that uncope and they choose to misused of methamphetamine to dealing with the stress that can excerbate psychotic symptoms if they use in high level and leading to poor social functioning. However, their self-efficacy in taking antipsychotic drugs would be a strong predictor and may decrease of both positive and negative psychotic symptoms, particularly social withdrawal and social dysfunction in schizophrenia due to the balance neurotransmitters (20-22). In contrast, stressful life events can destroy the medication-taking self-efficacy, if they had in effective coping with the stress or loss of social support. Similarly, to previous study, persons with psychotic symptoms can exacerbate and relapse influenced social dysfunction based on the principles of self-efficacy to increase the ability to look after themselves and manage diary physical activities: and to manage the stressful of social life events(10, 26). In another way, social support can improve social dysfunction by family member or significant other by support persons with schizophrenia and methamphetamine misuse to continuing taking medicine as doctor prescribe to decrease psychotic symptoms that help them to improve brain function in terms of cognitive , emotional, and behavior. This improvement will be positive effect on their activities function such as they can work, engage in the community activities, or perform their activities as usual.All of this is the improvement on the terms of social dysfunction (17).

The present study supports and extends previous findings that using methamphetamines significantly decreases the binding of dopamine and dopamine transporters in the striatum, a brain area that is important for both of memory and movement. Additionally, biological stressors can make individual non-medication adherents. Importantly, this behavior is the result of dopaminergic stressor that leads to the changes of cognitive function (poor judgment, loss of insight, disorganization, and paranoia) (27-29). Therefore, medication use and self-efficacy can decreased psychotic symptoms and social dysfunction might due to the balancing of psychotropic drug use (11, 23, 30-31) that effect on neurotransmitter to improve brain function and enhance their social function (10, 20, 22).

Interestingly, the moderation effects tested in the present study indicate that the social dysfunction is moderated by both medication use self-efficacy and psychotic symptoms was significantly positive at high levels. However, in the part of psychotic symptoms, this study aligns with previous research indicating that illicit methamphetamine use can precipitate and exacerbate positive symptoms in schizophrenia. Schizophrenic dopamine hypothesis describe that over activity of dopaminergic neurotransmission in mesolimbic pathways results in positive psychotic symptoms of schizophrenia. Methamphetamine use also induces the release of dopamine and can result in dopaminergic sensitization in chronic users: this occurs when excessive stimulation of the dopamine system increases hyper-reactivity to further pharmacological or environmental dopaminergic triggers such as stressful life events. This positive feedback mechanism prompts cumulative dopamine dysfunction in individuals with schizophrenia. Higher rates of racing thoughts in past-year users may be attributable to the direct acute effects of amphetamine intoxication, which are widely observed in individuals without a history of psychotic disorders and influence social dysfunction (17, 32-36).

VII. Conclusions

Social support had direct effect on medication-taking self-efficacy and stressful life events. Both of actions had direct and indirect effects on social dysfunction, respectively. The actions need an effective treatment plans awareness with the involvement from family and social support to all eviate patient's social dysfunction. They need more stress management skills, social support and they have to continue taking medicine in order to improve social dysfunction and decrease psychotic symptoms.

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Conflicts of Interest:
None.

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Photobiomodulator Effect on Fibromyalgia Stabilization in the Oncoterapeutic Process

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Abstract- In this case study, Photobiomodulation was used in the craniofacial and systemic region for the symptomatic control in patients with Fibromyalgia (fibrositis syndrome or fibromyositis), simultaneously with oncoterapic therapy through the specific hormone (Tamoxifen-TMX). This non-invasive and low-cost planning emerges as an alternative in the systemic recovery of patients with this syndrome at Hospital of Câncer de Ribeirão Preto.

Keywords: *fibromyalgia, photobiomodulation, laser therapy, oncology, cancer, dentist, hormone.*

GJMR-F Classification: *NLMC Code: WE 544*

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Photobiomodulator Effect on Fibromyalgia Stabilization in the Oncoterapeutic Process

Ms Juliano Abreu Pacheco [α], Dr. José Israel Sanchez Robles [σ], Dr. Cláudia Conforto de Sá [ρ] & Ms Guilherme Luna Martinez [ω]

Abstract- **In this case study, Photobiomodulation was used in the craniofacial and systemic region for the symptomatic control in patients with Fibromyalgia (fibrositis syndrome or fibromyositis), simultaneously with oncoterapic therapy through the specific hormone (Tamoxifen-TMX). This non-invasive and low-cost planning emerges as an alternative in the systemic recovery of patients with this syndrome at Hospital of Câncer de Ribeirão Preto.**

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I. Introdution

Fibromyalgia is a syndrome characterized by the presence of a wide range of symptoms that directly influence multiple systems in the body promoting a difficulty to designate it into a specific systemic category. It is usually manifested by generalized and persistent pain, abnormal sensitivity to pain, and additional symptoms such as fatigue, sleep disturbances, and mood symptoms (1-2). However the pathogenesis is controversial, but can be attributed or suggested by stress or idiopathic psychological factors. It was initially known as fibrositis, from which it evolved to the current specification of the term Fibromyalgia (FM), due to the symptoms of continuous or intermittent pain observed in patients with these generalized pain charts (3), and greater susceptibilities to comorbid psychiatric disorders (1-2). Research has come over the years that changes in the production of the hormones serotonin and epinephrine have fostered a possible etiology for triggering Fibromyalgia since the tricyclic antidepressants and selective serotonin antidepressants used in treatment therapy alter the balance that would provide the etiology of the disease. It is possible that the abnormalities promoted in the hormonal pathways favor the damping of the afferent pain signals, causing an increase in the perception of pain (4). This syndrome affects 2% of the population with a high incidence of middle-aged women. And it usually overlaps with other functional somatic syndromes, such as chronic fatigue syndrome and temporomandibular joint dysfunction. But even associated with mood and anxiety disorders, research suggests that although functional somatic disorders are related and potentially interact with psychological conditions, they are independent (5). This generalized, deep tissue-sensitive somatic pain results from sensitization of neural pain pathways, without departing from variable combinations of fatigue, sleep disturbances, cognitive dysfunction, and psychological distress (6). However, it should be noted that musculoskeletal conditions such as temporomandibular dysfunction (TMD) (7) have a direct relation in mandibular compression during daily activities and rest in patients with Fibromyalgia (7-8), in whom the coexistence of these pathologies generates a clinical outcome of high complexity (9). Aerobic, strength and mixed training programs (combination of aerobics, strength and flexibility) have been shown to reduce pain, number of sensitive points, fatigue, depression and anxiety, and improved health-related quality of life as well as functional capacity (10-11). Dental activities directed to the facial skull region are indicated for the treatment of Temporamandibular Dysfunction (TMD) as a procedure combined with other therapies such as electrotherapy, physiotherapy, temporomandibular joint mobilization and facial massage to reduce pain (12-13) . DTM is a dysfunction that is difficult to control and treat due to external factors that act as a complicating psychosomatic signal that contributes to the chronicity of the (systemic) fibromyalgia picture. In the new nuances of treatments, the use of a non-invasive therapy (photobiomodulation = laser therapy) emerges as a noble auxiliary resource, since it has the capacity to interact with biological tissues, and can trigger bioenergetic and cellular and molecular proliferative effects, whose primary photoreceptors are located in the mitochondrial respiratory chain (14-15) contributing with punctual analgesic and anti-inflammatory responses, reaching satisfactory muscle relaxation (16). Phototherapy using the low-intensity laser (LIB) and light-emitting diode (LED) therapy are being performed in patients with painful syndromes, including Fibromyalgia and Temporomandibular Dysfunction TMD (17). LIB contributes to the modulation of various

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signaling pathways and physiological mechanisms involved in analgesia (18-19). Research suggests that photobiomodulation increases the levels of β-endorphin, lymphatic flow and blood supply, as well as reducing bradykinin, releasing histamine, swelling, molecules associated with pain and inflammation, which leads to muscle relaxation (20-21). And it also corroborates with the therapeutic foundation, elucidated in the research that treated a group of patients with the low power laser protocol, of which the group exposed to the laser showed a greater decrease of pain than the group that did not undergo this phototherapy, supported by the image examination, through the monopotonic emission computed tomography (SPECT) of the involved ATMs (16). Already in this case study of Ribeirão Preto Cancer Hospital, we will address a patient who is a carrier of FM, but also uses adjuvant hormone (TMX-Tamoxifen) for breast cancer in the post-cycle of chemotherapy. This hormone has a significant reduction of 47% in the risk of recurrence and 26% in the risk of death (22). However, among the side effects of this drug, one of them is joint stiffness and / or pain similar to the feeling of recurrence of arthritis in several joints at the same time. This situation is most worrying, since joint pain can lead to the interruption of this therapy, which is so effective in controlling the disease (23). In a comparative study of therapies with patients receiving tamoxifen, most had joint symptoms, which were mild to moderate in severity, eliminating the need for treatment withdrawal. They observed that the most appropriate intervention for pain management in TMX-associated arthralgia may be a combination of changes in lifestyle, such as weight training, smoking cessation, moderation in alcohol consumption, dietary supplement intake of calcium and vitamin D for bone protection, and pharmacological options (24) (Table 1).

Table 1: Pharmacological Options, Source (24)

Opções farmacológicas para melhoria da dor em pacientes com câncer de mama inicial com sintomas de artralgia

Medicação	Dosagem
Acetaminofeno [a]	≤daily (considere ER.)
NSAID [a]	Naproxeno: 500–750 mg por dia (analgesia) 1000–1500 mg por dia (inflamação)
Inibidores da ciclooxigenase [a]	Celecoxib: 100-200 mg por dia [b]
Tramadol	≤400 mg por dia (considere ER.)
Narcóticos	Codeína versus oxicodona
Modificadores de dor	TCA : nortriptilina 10-100 mg por dia gabapentina, pregabalina
Esteróides intra-articulares	Acetato de metilprednisolona, suspensão de triancinolona: 40 mg / cm ^{3}

[a] Mínimo 2 semanas a dose tolerada.
[b] Máximo 400 mg por dia.
NSAID = medicamento anti-inflamatório não esteróide; ER = liberação prolongada; TCA = antidepressivo tricíclico.

Phototherapy (systemic) through the Intravascular Irradiation off blood (Ilib), triggers an antioxidant system composed of enzymes, the main one, SOD ZnCu, is the largest antioxidant agent (25) that we have and fifth enzyme in volume in the human organism. However, according to a recent review, evidence suggests that the enzymes catalase peroxidase and ceruloplasmin also absorb the red laser which potentiates other enzymes, which obviously further increases the antioxidant property of these enzymes when irradiated in the Ilibprocess .And these therapeutic effects of light may minimize the side effects caused by chemotherapeutic, hormone therapy and radiation therapy sessions as an important reduction in inflammation and pain.

II. Case Report

A 53-year-old white female EMGH diagnosed with multifocal invasive right breast carcinoma in 2013. Tumorectomy and lymphadenectomy of axillary lymph nodes were performed in the same year, followed by chemotherapy (QT) - 4 cycles (Taxol), Radiotherapy that ended in October 2013. Patient made use of Gabapentin 300mg oral and Tamoxifen with clinical symptoms of hot flushes, moderate hepatic steatosis and Fibromyalgia (FM). In October 2017, he presented to the Dentistry Service of the Hospital do Câncer to diagnose and monitor the reflexes arising from oncological therapies. The initial consultation revealed deficiency in oral hygiene, incipient xerostomia, dysgeusia and muscular fatigue in the bilateral face region. The patient underwent physical therapy at the same hospital once a week. The central object of this study was to perform the controlled phototherapy in the region in the external region of the face by noting the Temporal, Masseter and articular capsule (TMJ) muscles in a noninvasive way at the Cancer Hospital of Ribeirão Preto (SP), through the XT laser, DMC brand, useful red emitter laser power: 100 mW ± 20%, red laser wavelength 660 nm ± 10 nm, photobiomodulator effect, with specific protocol, and use of the Intravascular Laser Irradiation of Blood (IR) function in the radial artery of the wrist as complementary action. This radiation emitted by Low Power Lasers (LBP) has shown analgesic, anti-inflammatory and healing effects and is therefore widely used in the tissue repair process due to the low energy densities used and wavelengths capable of penetrating in tissues (26-27). Currently, this Low Intensity Laser (LBI) is being used for the overall recovery of the patient in several specialties of the health area; and their responses are considered to be beneficial (28-29) in a variety of different modalities due to their photobiomodulatory effect (30). Specifically, this mechanism when triggered in the craniofacial region is related to "neuronal repair and in neurogenesis, "not only in the formation of new brain cells, but also in" synaptogenesis, "which is the formation of new connections between existing brain cells (31). Therefore, it should be noted that the systemic and localized conditions during cancer treatment therapy contribute to the symptomatology of arthralgias, and in this niche of patients who use chemotherapy drugs and hormone

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therapy these functions are altered with a certain frequency influencing negatively well-being organic and emotional. When it acts at the cellular level, the low power laser causes biochemical, bioelectric and bioenergetic modifications, influencing the increase of metabolism, cell proliferation and maturation, the amount of granulation tissue and the decrease of the inflammatory mediators, inducing the healing process (32-33). And when the molecule is absorbed by light, it allows an increase in cellular metabolism, characterized by stimulation of photoreceptors in the mitochondrial respiratory chain, changes in cellular ATP levels, release of growth factors and collagen synthesis (34-35). This complementary function, Ilib, has triggered an antioxidant system composed of enzymes, and the main Zn Cu SOD is the largest antioxidant agent (36) that we have and fifth volume enzyme in the human body and is more resistant to variations in temperature and to denaturation by substances like guanidine chloride, sodium duodecil sulfate, or urea. That is, several enzymes in our body absorb the red laser which potentiates other enzymes, improving the antioxidant function of these enzymes when irradiated in the ILIB process. And these therapeutic effects of light can minimize the side effects caused by the chemotherapeutic, hormone-therapeutical and radiotherapeutic sessions.

a) *Clinical Conduct (Therapy[1])*

i. Hygiene of the oral cavity with clorexidine 0.12 % by digital friction, using the sterile gauze.
ii. Measurement of pain[2] (Table 2).
iii. Application of the Low Intensity Laser[2] (LIB) laser XT, DMC brand, useful red emitter laser power: 100 mW ± 20%, red laser wavelength 660 nm ± 10 nm, 1joule (10 seconds) - red / infrared 10 seconds in bilateral marked muscles) - figure a, e.
iv. Complementary 15-minute photoenteral therapy (Ilib) in the radial artery of the wrist.

[2]The measurement of pain was permeated by the Behavioral Pain Scale (EC):

Table 2: Pain Measurement[1]: Behavioral Pain Scale (EC) / Source (37)

Nota zero	Dor ausente ou sem dor
Nota três	Dor presente, havendo períodos em que é esquecida
Nota seis	A dor não é esquecida, mas não impede exercer atividades da vida diária
Nota oito	A dor não é esquecida, e atrapalha todas as atividades da vida diária, exceto alimentação e higiene
Nota dez	A dor persiste mesmo em repouso, está presente e não pode ser ignorada, sendo o repouso imperativo

The patient was monitored periodically for 4 months according to the table below (Table 3), through the proposed localized Lib protocol (Figure a), and simultaneously with Ilib therapy (Figure (b)) permeating the indoctrination proposed by the student Dr. Adriana shaposhink on "patient management" that require a greater regulatory control to maintain the state of general health.

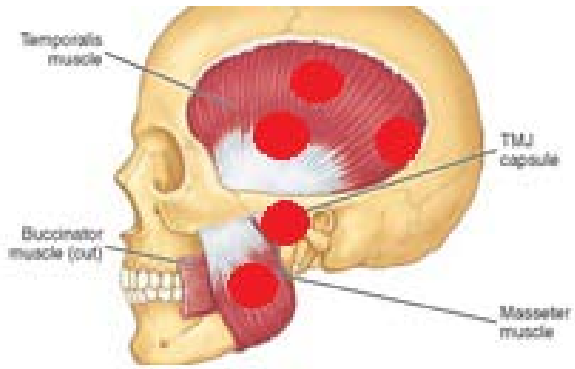

Fig1: Points of Application of the Lib

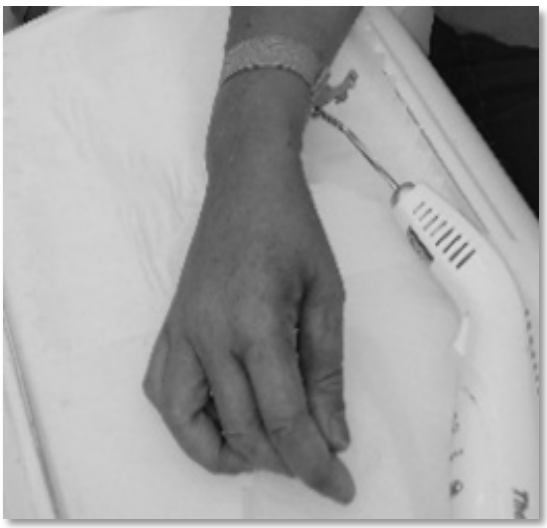

Fig. 2: Ilib in the Radial Artery of the Right Wrist / Fonte Hospital Câncer Ribeirão Preto

The results obtained were increasing until they reached the normalization of the sensory function previous to the proposed period initially, according to the table (Table 3) below:

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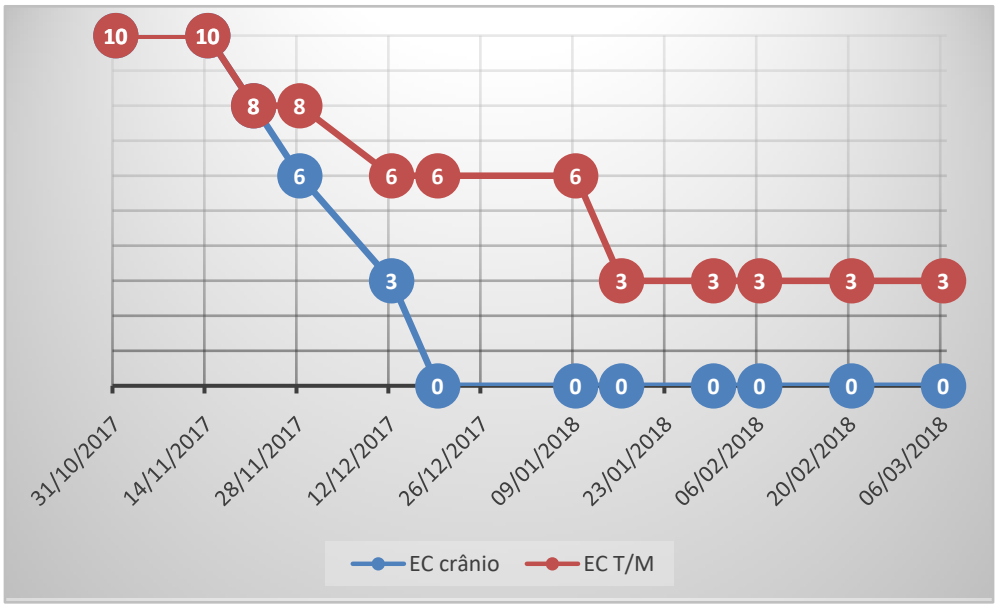
Table 3: Cronologia dos Protocolos Propostos Para Utilização do Lib e Ilib.

Date	Therapy[1]	Craniofacial Pain	EC [1]	Trunk Pain / Limbs	EC [2]
31/10/2017	Lib / Ilib	Sim	10	Sim	10
14/11/2017	Lib / Ilib	Sim	10	Sim	10
21/11/2017	Lib / Ilib	Sim	8	Sim	8
28/11/2017	Lib / Ilib	Sim	6	Sim	8
12/12/2017	Lib / Ilib	Sim	3	Sim	6
19/12/2017	Lib / Ilib	Não	0	Sim	6
09/01/2018	Lib / Ilib	Não	0	Sim	6
16/01/2018	Lib / Ilib	Não	0	Sim	3
30/01/2018	Lib / Ilib	Não	0	Sim	3
06/02/2018	Lib / Ilib	Não	0	Sim	3
20/02/2018	Lib / Ilib	Não	0	Sim	3
06/03/2018	Lib / Ilib	Não	0	Sim	3

EC[1] / EC[2]:Measurements performed before the phototherapy intervention.
Therapy[1]: Suggested clinical conduct.

III. Discussion

In this study, the initial proposal was to promote a noninvasive dosing through local and systemic photobiomodulation aiming at an improvement of the pain picture in the facial and general region caused by fibromyalgia. The results obtained after the first and second applications of the laser (lib and ilib) did not change the condition, but from the 3rd application there was a decrease in pain in both the facial and trunk / limb regions, even with simultaneous hormone therapy. This evolution produced a greater balance in the habitual activities of the patient and a fundamental impact on the self-esteem which allowed an improvement in the resumption of the quality of life. The positive sequence in EC[1] compared to EC[2], a trend that became increasing in the 10 subsequent consultations until reaching an acceptable level in the Level 3 Behavioral Scale (EC), which made it relevant for a fibromyalgia syndrome in association with TMX. In addition to this, the support that phototherapy demonstrates in exercising healthy cellular activity, an increase in cellular metabolism, improves cellular regeneration, invokes an anti-inflammatory response, promotes the reduction of edema, reduces the formation of fibrous tissue, stimulates the function reduces the production of substance P, stimulates the long-term production of nitric oxide, decreases the formation of bradykinin, histamine and acetylcholine, and stimulates the production of endorphins (38).And the following graphic elucidates the treatment of pain until the neutralization in the facial skull region (EC skull) and acceptable stage in the trunk and limb regions (EC T/M or P/L):



Source: Hospital Câncer Ribeirão Preto

Chart 1: Initial and Final Stage

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IV. Conclusion

The clinical evolution of this specific case is undeniable through photobiomodulation, and it is important the multidisciplinary involvement of all the staff in their various specialties that contributed in an assertive way to stabilize the picture. Although the clinical results look very promising, and the low-power laser fits perfectly into the realm of "high-tech" therapy, care must be taken not to regard it as a new panacea. The ideal that this technology continues to perpetuate advances in this topic of pain control related to fibromyalgia, from which the systemic repercussions potentiate benefits irradiated to other sites fundamental to the maintenance of health. The biomedical effects of low power laser irradiation were investigated in several health areas. Beneficial effects such as immunosuppression, immunostimulation, autoimmune disease and nerve regeneration have been described and gain strength as a new therapeutic modality, due to the recognition as a viable treatment option for a diverse range of diseases and conditions characterized by injury, degeneration, inflammation and pain (39). But it is important to emphasize that the goals of containment of the disease have been reached and reiterate the need to permanently manage these patients affected by fibromyalgia and who are still undergoing oncoterapias. to control the disease. And I stress that "Laser was not able to replace many of today's techniques and physical modalities, however, it can be used together to improve the health of patients (40)."

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hsCRP and E-Selectin as Markers of Endothelial Dysfunction in Children with Type 1 Diabetes Mellitus

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Abstract- *Introduction:* This study investigated the levels of inflammatory biomarkers in healthy children and those diagnosed with type 1 diabetes (T1DM), some of whom were affected by endothelial dysfunction (ED), characterized by increased inflammation and reduced vasodilatation.

Methods: Thirty-one T1DM children showing no symptoms of vascular diseases and diagnosed by ultrasound techniques as ED-positive (T1DM-ED) or negative (T1DM), and 58 sex-age-matched healthy children were investigated for circulating levels of E-selectin, s-ICAM and s-VCAM, MMP-9, high-sensitivity C-reactive protein (hsCRP), and IL-6.

Results: No differences were observed in s-ICAM, MMP-9, and IL-6 levels between case and control groups. Significantly higher levels of s-VCAM ($p = 0.0001$) were found in the T1DM (1359.1 ± 273 ng/mL) and T1DM-ED (1358.2 ± 112 ng/mL) groups; (control - 828.5 ± 212 ng/mL). Higher levels of E-selectin ($p = 0.001$) were found in the T1DM-ED group (331.2 ± 77 ng/mL); (control - 222.2 ± 74 ng/mL). The values of hsCRP were higher ($p = 0.002$) in the T1DM-ED group (0.36 ± 0.2 mg/L) relative to control (0.15 ± 0.1 mg/L) and T1DM (0.19 ± 0.2 mg/L). The results suggest that E-selectin and hsCRP can be useful markers of ED in children with T1DM.

Keywords: *type 1 diabetes mellitus, children, endothelial dysfunction, markers, E-selectin, hsCRP.*

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hsCRP and E-Selectin as Markers of Endothelial Dysfunction in Children with Type 1 Diabetes Mellitus

Markers Laboratory of Endothelial Dysfunction

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Keywords: type 1 diabetes mellitus, children, endothelial dysfunction, markers, E-selectin, hsCRP.

I. Introduction

Type 1 diabetes mellitus (T1DM) is a complex metabolic disorder characterized by chronic hyperglycemia due to a complete lack of insulin secretion [1]. The constant hyperglycemic state associated with the increase in circulating free fatty acids trigger molecular mechanisms that lead to a decrease in nitric oxide (NO) bioavailability, increased oxidative stress, increased expression of pro-inflammatory and prothrombotic factors, and reduced vasodilatation, promoting endothelial dysfunction [2].

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Endothelial dysfunction (ED) precedes the cardiovascular complications that are the leading cause of death in diabetic patients. Nephropathy, retinopathy, and neuropathy are some of the most common microvascular complications, where as cardiovascular disease, peripheral arterial disease, and stroke are the main macrovascular complications. Currently, ED has gained attention as a predictor of T1DM-related vascular diseases [3].However, little is known about the early stages of vascular alterations in children with diabetes.

In recent years, several molecules are being considered new biomarkers of ED, such as VCAM-1 (vascular cell adhesion molecule-1), ICAM-1 (intercellular adhesion molecule-1), and E-selectin. These molecules are involved in the adhesion of leukocytes to the vascular wall and are associated with endothelial dysfunction, retinopathy, albuminuria, and coronary disease [4,5]. Several studies have suggested that these molecules are present in higher levels in patients with diabetes [6,7,8,9,10].

Other important molecules involved in ED are matrix metalloproteinases (MMPs), endopeptidases that are secreted by macrophages and act in the degradation and remodeling of extracellular matrix components, such as collagen, proteoglycans, elastin, fibronect in, and other glycoproteins [10,11,12]. In diabetes, high glucose levels lead to changes in MMP regulation, altering the balance between the synthesis and degradation of matrix components [13]. MMP-9 is an essential molecule for vascular remodeling, and studies indicate that this metalloproteinase is involved in the formation and destabilization of atheromatous plaques [10,14] and in ischemic stroke [15]. Other studies have shown higher levels of MMP-9 in patients with diabetic complications [16], including children [17].

Moreover, C-reactive protein, produced and released by hepatocytes after stimulation by interleukins IL-1 and IL-6, plays an important role in ED: it reduces eNOS messenger RNA transcription and NO formation, increases the release of ET-1 and IL-6, and induces the release of adhesion molecules and

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chemotactic cytokines [18]. It has previously been shown that CRP and IL-6 are associated with T1DM-related cardiovascular events and microangiopathy [19].

Circulating biomarkers such as E-selectin, soluble ICAM and VCAM, MMP-9, CRP, and IL-6 play a significant role in ED. Consequently, they may contribute to both the early diagnosis of the inflammatory process involved in ED and the development of new therapeutic strategies [20]. The aim of this study was to investigate the association of these markers with the presence or absence of ED in children with T1DM.

II. Material and Methods

a) Study Participants

The study included 31 children with type 1 diabetes mellitus, from 6 to 12 years old (mean age: 8.36±1.8 years), and 58 age- and sex-matched healthy children, also between the ages of 6 and 12 (mean age: 6.9±1.7 years), designated as the control group. Children with T1DM were treated at the Pediatric Endocrinology Outpatient Clinic at the Brasilia University Hospital and at the Pediatric Clinic of the Brasilia Children´s Hospital. The children in the control group were recruited among relatives of hospital staff involved in the study.

All children with T1DM included in the study underwent detailed physical examinations (which included blood pressure and skin sensitivity monitoring), biochemical blood and urine tests (including complete evaluation of renal function and microalbuminuria), and complete ophthalmic examination, all under the supervision of a pediatric endocrinologist. Children in the control group had normal height and weight for their age, according to the Center for Disease Control and Prevention's (CDC) guidelines [21](adapted to Brazilian children) [22]. They all had fasting glucose levels <100 mg/dL, and glycated hemoglobin (HbA1c) ≤5.6%.

Exclusion criteria for both groups were onset of puberty, evidence of hypertension, dyslipidemia (total cholesterol ≥ 200 mg/dL, HDL <45mg/dL, LDL≥130 mg/dL, VLDL ≥ 41mg/dL, triglycerides ≥100 mg/dL for children aged up to 10 years old, or triglycerides ≥130 mg/Dl for children older than 10), family history of primary dyslipidemia and premature death due to cardiovascular or cerebrovascular disease, presence of anemia (hemoglobin <11 g/L and hematocrit <33%), presence of acute infectious conditions or chronic conditions other than diabetes mellitus, and continued use of medications other than insulin.

The study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Parents or legal guardians of the children participating in the study signed an informed consent form. The study was approved by the University of Brasilia's College of Health Science's (CEP-FS) Research Ethics Committee.

The children were divided into three groups according to the presence of type 1 diabetes mellitus and endothelial dysfunction: healthy children (control), Children with T1DM and no endothelial dysfunction (T1DM), and children with T1DM and presenting endothelial dysfunction (T1DM-ED).

b) Laboratory Analysis of Biomarkers

Serum samples were collected after 8 h of fasting, according to the H3-A6 standard of the Clinical and Laboratory Standards Institute (CLSI) [23] in serum separator tubes. Samples were centrifuged at 3000 rpm, and the serum was stored at -2°C until used for measuring the levels of high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), endothelial selectin (E-selectin), soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), and the marker of vascular damage matrix metalloproteinase-9 (MMP-9). The method of measurement and the equipment used are summarized in Table 1.

Table 1: Methods and Equipment used for Determining Serum Levels of each Marker

Marker	Equipment and Manufacturer	Method
sE-selectin	BEST 2000 ELISA System (Werfen group, Barcelona, Spain) IBL International ELISA Kit (IBL, Hamburg, Germany)	Direct Sandwich ELISA
sICAM-1	BEST 2000 ELISA System (Werfen group, Barcelona, Spain) IBL International ELISA Kit (IBL, Hamburg, Germany)	Direct Sandwich ELISA
sVCAM-1	BEST 2000 ELISA System (Werfen group, Barcelona, Spain) IBL International ELISA Kit (IBL, Hamburg, Germany)	Indirect Sandwich ELISA
MMP-9	BEST 2000 ELISA System (Werfen group, Barcelona, Spain) IBL International ELISA Kit (IBL, Hamburg, Germany)	Indirect Sandwich ELISA
hsCRP	BN II System (Siemens®, Marburg, Germany)	Nephelometry
IL-6	BEST 2000 ELISA System (Werfen group, Barcelona, Spain) IBL International ELISA Kit (IBL, Hamburg, Germany)	Indirect Sandwich ELISA

c) Statistical Analysis

We performed statistical analyses using version 5.0 of the Graph Pad Prism software (Graph Pad Software, San Diego, California, USA). One-way ANOVA and Dunnett or Bonferroni post-hoc tests were used for comparisons between control and groups T1DM/T1DM-

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ED and between T1DM and T1DM-ED, respectively. Differences were considered statistically significant when $p \leq 0.05$.

III. Results

In a previous study by our research group [24], ultrasonographic techniques were used to measure the flow-mediated dilation (FMD) of the brachial artery and the thickness of the intimal and medial layers (IMT) of carotid arteries in order to investigate the presence of ED in children with T1DM. Results showing decreased vasodilator response, indicative of endothelial dysfunction, were found only in children who were diagnosed with T1DM at least five years prior to the study. These children were included in the T1DM-ED group of the present study, while children without ED were included in the T1DM group.

To assess the presence of markers indicative of vascular remodeling, serum levels of the MMP-9 enzyme were measured in the control and the groups of children with diabetes. T1DM and T1DM-ED patients presented MMP-9 serum levels similar to the control group (control 35.7±4 ng/mL;T1DM 35.4±2 ng/mL;T1DM-ED 36.5±1 ng/mL), with no statistical differences between them (Fig. 1A).

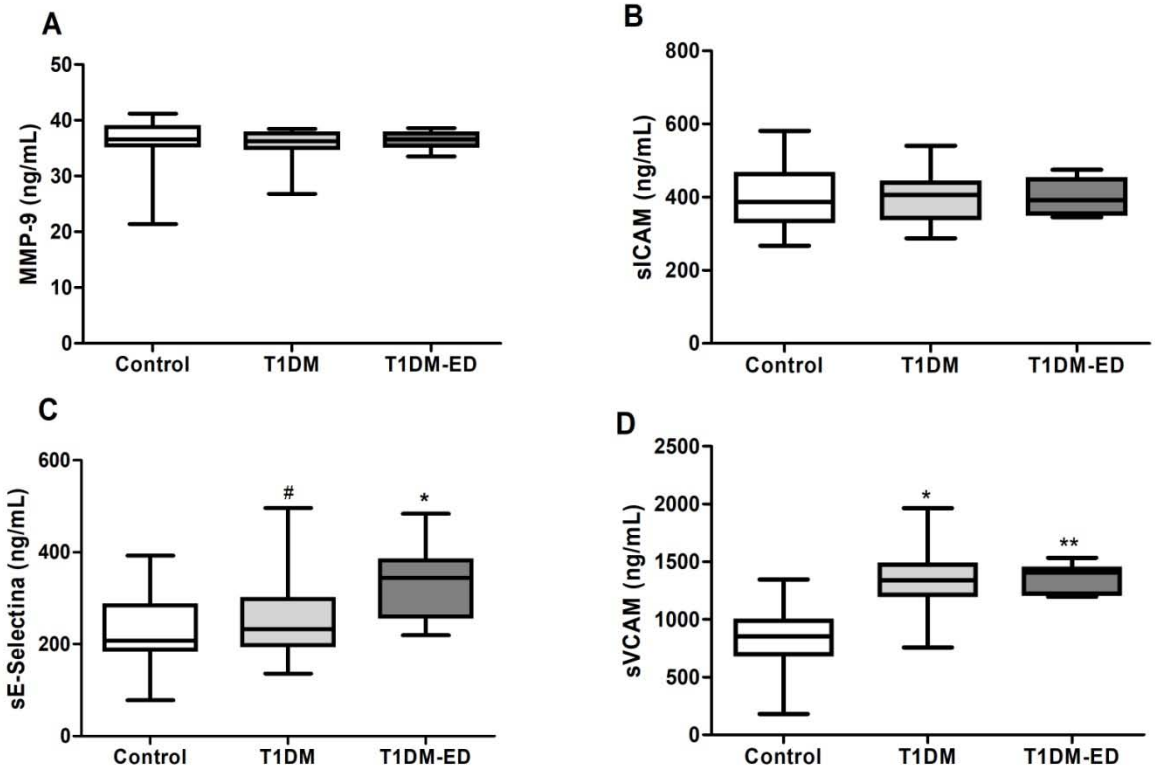

Fig. 1: Serum levels of each biomarker (1A) MMP-9 and (2A) sICAM showed no statistical differences between control and diabetic groups. (1C) E-selectin was significantly higher in T1DM-ED (*p = 0.001) than in the control (Dunnett's post-hoc test) and in T1DM (#p = 0.001): (1D) sVCAM was elevated (* and **p = 0.0001) in both groups of diabetic patients, with and without ED. Results were analyzed using one-way ANOVA and Dunnett's post-hoc test.

Serum levels of E-selectin, sVCAM-1, and sICAM-1 were also investigated. Patients with diabetes had similar sICAM-1 levels to subjects in the control group, with no statistical differences between control (398.1±81 ng/mL), T1DM (394.1±56ng/mL), or T1DM-ED (416.2±44ng/mL) (Fig. 1B).

Significantly higher levels of E-selectin ($p = 0.001$) were found in T1DM-ED (331.2±77 ng/mL) when compared to the control (222.2±74 ng/mL), whereas levels in T1DM (244.4±81ng/mL) did not differ significantly from the control (Fig. 1C). In contrast, increased levels of sVCAM-1 ($p = 0.0001$) were found in both DM groups (T1DM 1,359.1±273 ng/mL; T1DM-ED 1,358.2±112 ng/mL)in comparison to the control (828.5±212 ng/mL) (Fig. 1D).

Serum levels of IL-6 and hsCRP were measured to verify the presence of an inflammatory state in individuals with diabetes. Serum levels of IL-6 were within reference values and presented no statistically significant differences between control (0.99±0.5 ng/mL), T1DM (1.13±0.6 ng/mL), and T1DM-ED (0.83±0.2 ng/mL) (Fig.2A).

However, elevated hsCRP levels were observed in DM groups. The values were 0.15±0.1 mg/L for the

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control, 0.19±0.2 mg/L for T1DM, and 0.36±0.2 mg/L for T1DM-ED. Values were significantly higher (p = 0.002) in the T1DM-ED group than in the control group (Fig. 2B). This result indicates the presence of an inflammatory state in children with endothelial dysfunction.

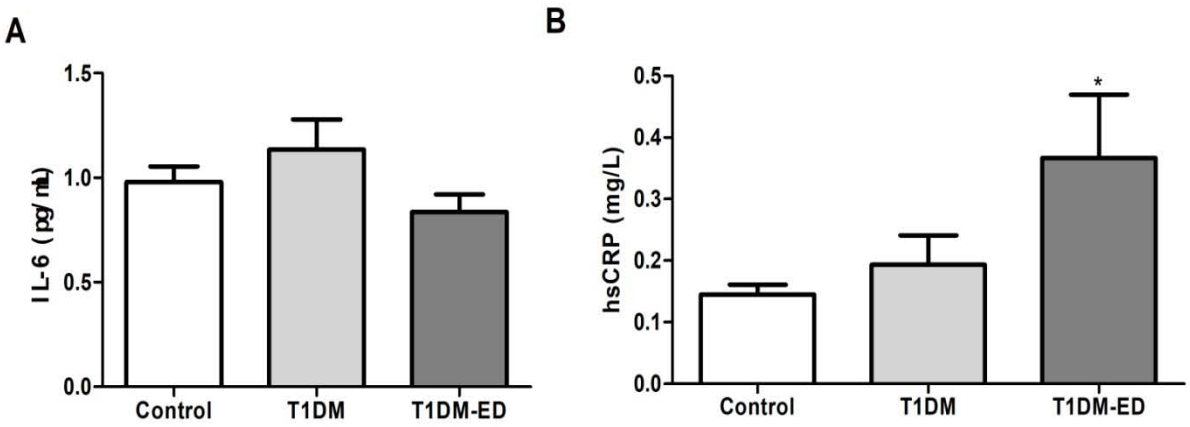

Fig. 2: IL-6 (A) and hs-CRP levels (B) in control and diabetic groups Results were analyzed using one-way ANOVA and Dunnett's post-hoc test, comparing control and T1DM-ED for hs-CRP (*p = 0.0026).

IV. Discussion

Diabetes mellitus is one of the most prevalent chronic diseases affecting children and adolescents. The World Health Organization (WHO) estimates that diabetes will represent the seventh leading cause of death worldwide by 2030 [25]. Vascular alterations are the main cause of morbidity and mortality in patients with Type 1 diabetes mellitus, including children and adolescents [26, 27]. Endothelial dysfunction has been shown to precede vascular alterations and can be used as an early predictor of cardiovascular diseases [28].Endothelial cells actively regulate vascular tonus and reactivity under physiological and pathological conditions, responding to mechanical stimuli and neurohumoral mediators with the release of a variety of vascular relaxing/constricting factors and synthesizing substances that regulate inflammation and homeostasis. As the actions of endothelial cells may affect several systems, either simultaneously or sequentially, a gold standard test for evaluation of endothelial dysfunction has not yet been established [29].Endothelial function is usually estimated by variations in blood flow or arterial vessel diameter in response to mechanical or chemical stimuli, evaluated invasively, through coronary catheterization, or non-invasively, through ultrasound examinations, such as measurement of FMD of the brachial artery and IMT of carotid arteries [29].Despite being non-invasive, these tests require time, equipment, and skilled personnel, not always readily available in health services. On the other hand, laboratory tests based on blood samples are usually faster and cheaper and could serve as tools for the early prevention of cardiovascular complications. Among the various molecules known to participate in ED, hsCRP, IL-6, sICAM-1, sVCAM-1, E-selectin, and MMP-9 were investigated as potential biomarkers in children with Type 1 diabetes mellitus in this study.

The majority of the data available on markers of endothelial dysfunction come from studies in adult patients with Type 2 diabetes mellitus (T2DM). Furthermore, most of theT1DM data available have been obtained from adult patients and/or patients who already showed vascular complications [9,30]. Data on T1DM patients, especially children, are still scarce. The present study evaluated children with T1DM with and without ED who did not present vascular diseases and healthy children as control.

Monitoring MMP-9 levels appears to be useful to predict microvascular complications in T1DM. The hyperglycemic medium induces an increase in its levels [31], which are in accordance with the progression of diabetes and the severity of complications [32]. In children with T1DM (5 to15 years old) a substantial increase in MMP-9 levels in lacrimal samples was associated with progression of diabetic retinopathy as well as localized pathological remodeling [33]. In subjects with T1DM (4 to 40 years old) with sub-optimal glycemic control (HbA1c 8.3% ± 1.8),the level of this marker was notably high in urine samples and correlated positively with HbA1c levels and disease duration, suggesting that its levels may function as a marker of latent nephropathy, prior to clinically defined microalbuminuria [34].

However, serum levels of MMP-9 do not seem to be an indicator of the endothelial dysfunction that precedes vascular complications. Lee et al [35] reported no increase in MMP-9 levels in the serum of T2DM adults diagnosed up to 3 years prior to the study and no complications. Our results indicate that, even in children

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with T1DM and more than five years of disease duration, there was no change in MMP-9 levels when vascular complications were not present since serum levels of MMP-9 were similar in children with and without ED.

Atherosclerosis is considered an inflammatory disease, because a low-grade inflammatory state contributes to all stages of its development, starting with endothelial dysfunction, up to plaque formation and rupture and the thrombotic complications that follow [28].Cell adhesion molecules mediate the migration of large numbers of leukocytes (selectins) and their adhesion to the endothelium (VCAM-1 and ICAM-1). These molecules are involved in establishing an inflammatory process and can be useful as markers of inflammation [36].

There are, however, inconsistencies in the results of studies with these markers, especially regarding ICAM and VCAM. Some studies found no correlation between ICAM and arterial stiffness or atherosclerosis [37] while others implicated only VCAM-1 [38] or only ICAM-1 [39]. In the present study, we did not find significant differences between sICAM-1 levels in T1DM children with and without ED and the control group. In contrast, sVCAM-1 levels were elevated in all children with diabetes when compared to the control, and, therefore, were associated with the presence of diabetes but not with endothelial dysfunction in our study population. Further studies should clarify the role of sICAM-1 and sVCAM-1 in ED.

On the other hand, more consistent results have been reported for E-selectin, since many studies have associated an increase in its levels and presence of diabetes [40], endothelial dysfunction [41] and elevated diastolic blood pressure values in T1DM children, even in those who had been recently diagnosed [42] or had no vascular disease [43]. Furthermore, the value of E-selectin concentration to evaluate the risk of atherosclerosis was evident by its association with worsening of risk factors, such as high blood pressure, glucose, and lipid levels [30].

In the present study, we demonstrated that elevated E-selectin values were associated with the presence of ED in children with Type 1 diabetes mellitus. The fact that E-selectin is produced exclusively by endothelial cells (EC) makes it an excellent marker for evaluating endothelial dysfunction in comparison to other cell adhesion molecules, such as ICAM-1 and VCAM-1,which are expressed both by EC and leukocytes [44].

The acute hyperglycemia and poor glycemic control in the initial stages of T1DM have been associated with increased inflammation, which persists for at least two hours after the correction of hyperglycemia [45,46].Elevated serum levels of IL-6 and hsCRP were related to high levels of HbA1c [45]. We found the highest levels of hsCRP in children that had shown elevated levels of HbA1c in a previous study ($p = 0.018$) [24] corroborating the association between hyperglycemia and inflammation.

Although serum levels of IL-6 and hsCRP have been used to infer subsequent development of atherosclerosis [47], the most promising marker of inflammation for clinical application appears to be hsCRP [48]because, in comparison with IL-6, it has a longer half-life, more stable serum levels, and no circadian variation [49]. The isolated change in hsCRP levels observed in the present study, with no alteration in IL-6 levels, may be due to the greater stability of the marker or the low-grade inflammation that occurs in stages preceding vascular damage. Nonetheless, the results confirm the utility of hsCRP as an early marker of ED.

V. Conclusions

The results reported herein suggest that hsCRP and E-selectin may be good markers of ED in pediatric patients. Currently, these markers are not routinely analyzed in laboratory tests, at least in Brazil [50]. Their inclusion in routine tests as indicators of ED could serve as a subsidy for early interventions for the prevention of vascular diseases. However, this study presents some limitations due to the small number of participants and lack of patient follow-up. Further studies are required to broaden the results presented herein.

Author´s Contributions:

Antonella Márcia Mercadante de Albuquerque do Nascimento performed the clinical evaluation of all patients and revised and organized all the laboratory data. Rosane Mansan Almeida performed the laboratory analyses, wrote part of the manuscript and revised it. Inês Jorge Sequeira performed the statistical analysis. Yanna Karla de Medeiros Nobrega conceived the study design, wrote part of the manuscript and revised it. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee of the respective country and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. This article does not contain any studies with animals performed by any of the authors.

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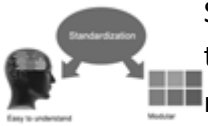

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Acknowledgments

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The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

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It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

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The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

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Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

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6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

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10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

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To make a paper clear: Adhere to recommended page limits.

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- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

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This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

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Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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