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Psychiatric Variables in *Cytomegalovirus* or *Toxoplasma gondii*—Infected Pregnants: Prospects for Cure with a Program of “Counseling about Behavioral Change”

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Abstract

TORCH complex, one of the potential infections that may occur during pregnancy, may contribute also to prenatal pregnant women’s anxiety and depression. The aim of this study was to explore the presence of psychiatric symptoms, in relation with infection of TORCH agents, specifically the *Toxoplasma gondii* (*T. gondii*) and Cytomegalovirus (CMV). The study was conducted on 58 pregnant women recruited from the Clinical Virology Unit, A.O.U. Policlinico-Vittorio Emanuele, P.O. “Gaspere Rodolico”, from September 2012 to March 2014. Psychiatric symptoms were evaluated through the Symptom Checklist-90 Revised (SCL-90 R) in pregnant women with CMV or *T. gondii* infection. Moreover, pregnant women were invited to participate in a program of “Counseling about behavioral change”, an effective psychotherapeutic training for the development of new motivational strategies to the infection acceptance, the greater self-confidence and greater adherence to treatment. The age of the subjects was positively correlated with Depression ($r = 0.119$, $p < 0.05$) and negatively correlated with Phobic Anxiety ($r = -0.178$, $p < 0.05$). The same variables were also negatively correlated with the level of education ($r = -0.231$, $r = -0.320$, $p < 0.05$) and with the dimension Somatization ($r = -0.208$, $p < 0.05$). Somatization was positively correlated with unmarried patients ($r = 0.141$, $p < 0.05$), while Phobic Anxiety was negatively correlated with unmarried patients ($r = -0.105$, $p < 0.05$). Somatization, Phobic Anxiety and Depression were po-

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sitively correlated with the variable “unemployment” ($r = 0.236$, $r = 0.218$, $r = 0.202$, $p < 0.05$). In relation to the type of infection, the dimension Anxiety was positively correlated with toxoplasmosis ($r = -0.236$, $p < 0.05$). Finally, we can notice an improvement of the variables Anxiety and Somatization in the whole sample after the attendance at the counseling psychotherapeutic program. Our study suggests the presence of anxiety and somatization in pregnant women with infection, expression of a phase of emotional fragility with the concern of transmitting a serious disease in the unborn child. The program “Counseling about behavioral change” allowed us to create an atmosphere of trust and to understand the usefulness of “empathic listening”. Giving correct and accurate information about the disease reassures the patient and prevents the realization of negative thoughts and further concern and discomfort.

Keywords

Pregnancy, Psychiatric Symptoms, Somatization, *Toxoplasma gondii*, Cytomegalovirus

1. Introduction

Prenatal depression and anxiety are common, temporary and treatable disorders experienced by women during pregnancy and in the first year after the birth of their child. They can affect any woman—regardless of age, race, income, culture or education [1]. However, family history, previous health or mental health problems, and stressful life circumstances—such as the presence of an infection—can increase a woman’s chances of having depression or anxiety.

In particular, an infection caused by the TORCH complex (*Toxoplasma gondii*, Others, Rubella, Cytomegalovirus, and Herpes simplex virus I and II) can impact on a woman’s psychological and emotional state, partially already compromised by the pregnancy [2]. Among the TORCH agents, those considered in this study are *Toxoplasma gondii* (*T. gondii*) and Cytomegalovirus (CMV), which might contribute to prenatal anxiety and depression [3].

T. gondii is of particular concern in humans because of the potential for transmitting the disease to the unborn fetus if the mother is infected during pregnancy [4] [5]. Toxoplasmosis most commonly manifests as a mild, flu-like illness with low-grade fever, myalgia, malaise, and headache, but primary infection in humans may also cause spontaneous abortion, fetal mental and psychomotor retardation, retinochoroiditis, encephalitis and hepatitis [6]. In order to prevent *T. gondii* infection, proper hygiene should be always maintained. In particular, hands should be washed thoroughly after handling raw meat. Moreover, pregnant women should stay away from strays and do not let pets wander because handling strays can cause toxoplasmosis.

Congenital CMV infection constitutes a major public health problem in developed countries because of its frequency and its role as a cause of sensorineural hearing loss (SNHL) and central nervous system damage in children [7]. The risk of intrauterine transmission after primary CMV infection during pregnancy approaches 40%, with an increased risk of adverse fetal effects if the infection occurs during the first and second trimester of pregnancy. Approximately 10% to 15% of the infected infants have symptoms at birth, including intrauterine growth restriction, petechiae and thrombocytopenia, jaundice, microcephaly, intracranial calcifications, chorioretinitis. Mortality in symptomatic infants is high (10% - 30%) and most of survivors develop cognitive, motor and visual deficits [8]. Pregnant women should take steps to reduce their risk of exposure to CMV and so reduce the risk of CMV infection of their fetus. In particular, in order to avoid exposure to saliva and urine that might contain CMV, they should wash their hands often with soap and water for 15 - 20 seconds, especially after changing diapers, feeding a young child, wiping a young child’s nose or drool, handling children’s toys. Moreover, pregnant women should avoid to share food, drinks, eating utensils with young children and should avoid contact with saliva when kissing a child.

The recent psychiatric nosology has provided a new diagnostic category, the so-called “Psychological factors that affect other medical conditions”. An essential feature to put this diagnosis is the presence of a close temporal relationship between psychiatric symptoms and the onset or exacerbation of a specific medical condition [9]. The first and most important step in the diagnosis is to listen to the patient, paying attention not only to her words, but also to the emotional involvement wherewith she refers to the symptoms and her behavior during the

interview [10]. It is important to investigate the underlying organic disorder and its severity to help the patient to manage the condition of alertness and apprehension that can worsen the mental and physical malaise. Unfortunately, the psychiatric symptoms related to the organic disease are often unrecognized and untreated, impacting the whole family [11].

Based on these assumptions, our study aims to explore the presence of psychiatric symptoms through the Symptom Checklist-90 Revised (SCL-90 R) in pregnant women with *T. gondii* or CMV infection [12]. Moreover, possible modifications of these symptoms through the participation to a psychotherapeutic program on “Counseling about behavioral change” were investigated.

2. Methods

2.1. Studied Population

The sample consisted of 74 patients with primary infection with *T. gondii* (48.6%) or CMV (51.4%) recruited from the Clinical Virology Unit, A.O.U. Policlinico-Vittorio Emanuele, P.O. “Gaspare Rodolico”, from September 2012 to March 2014. Sixteen patients were excluded from the study because they interrupted or followed the protocol provided in a discontinuous manner. Of the remaining 58 (78.4%) pregnant women included in the study, 27 (46.6%) were infected with *T. gondii* and 31 (53.4%) with CMV between the 12nd and the 18th gestational week.

The overall mean age was of 29.5 years. Nearly half of the enrolled women had a middle school education, while the others a low school education. Inclusion criteria were age ≥ 14 years and the ability to understand and to answer the questions asked. The exclusion criteria were the current presence of psychiatric disorders or use of drugs that could influence cognitive and emotional aspects during the psychic evaluation.

The study was approved by the institutional ethics committee and the patients agreed to participate by signing an informed consent.

The psychiatric symptoms of the enrolled patients were studied through the Symptom Checklist-90-Revised (SCL-90-R), which is a 90-item self-report symptom inventory developed by Leonard R. Derogatis in the mid-1970s [12]. The SCL-90-R assesses nine dimensions. Variables considered were: Somatization (SOM), Obsessive-Compulsive (OBS), Interpersonal Sensitivity (INT), Depression (DEP), Anxiety (ANX), Hostility (HOS), Phobic Anxiety (PHOB), Paranoid Ideation (PAR) and Psychoticism (PSY). All participants completed the questionnaire between the 12th and the 18th gestational week (T1) and three months after (T2). During this time—between T1 and T2—pregnant women were invited to participate to a program of “Counseling about behavioral change” which included 12 sessions lasting 60 minutes each. Each meeting was attended by 10 pregnant women.

The program was divided into three phases. Each phase consisted of four meetings. The first phase was dedicated to “empathic listening”, then providing detailed information on the infection and possible subsequent risks. The second step was the investigation of possible different treatment strategies and lifestyles to plan. In the third phase we worked on the possibility of creating motivation to change behaviour-problem, highlighting the commitment to change [13].

2.2. Serological Tests

The specific anti-*T. gondii* and anti-CMV IgG and IgM were assayed in serum with the semi-automatic ELFA method (VIDAS Toxo IgG II, Toxo IgM, CMV IgG and CMV IgM, bioMérieux sa, Marcy l’Etoile, France), which combines an inhibition-competition enzyme immunoassay method with a final fluorescent detection. The intensity of the fluorescence is inversely proportional to the concentration of antibodies present in the sample. The Solid Phase Receptacle (SPR) serves as the solid phase and reagents for each assay are ready-to-use and pre-dispensed in sealed reagent strips. All of the assay steps are performed automatically.

In brief, after dilution, each sample was incubated with the SPR. Anti-Toxoplasma and anti-CMV antibodies (IgM and IgG) present in the specimen were bound to the *T. gondii* and CMV lysate proteins coating the interior of the SPR. Unbound components were eliminated during the wash steps. The solid phase was then incubated with the conjugate, that competed with the antibodies coated on the interior of the SPR by the *T. gondii* and CMV antigens. Unbound conjugate was removed by washing. During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) was cycled in and out of the SPR. The conjugate enzyme catalyzed the hydrolysis of the substrate into a fluorescent product (4-Methyl-umbelliferone), the fluorescence of which was

measured at 450 nm. Results were automatically calculated by the instrument and expressed as an index in relation to the calibration curve stored in memory.

CMV and *T. gondii* IgG avidity assay was performed on IgG- and IgM-positive serum samples using Beia CMV/*T. gondii* IgG Avidity kit (Technogenetics s.r.l., Sesto San Giovanni, Italia) for the avidity detection of the specific IgG antibodies to CMV, according to manufacturer's instructions to detect primary infections.

2.3. Statistical Analysis

Data were examined for normality and transformed if necessary.

Pearson's R correlation test was performed using the 'Statistical Package for Social Sciences' (SPSS, Version 17). All data on pregnant women at T1 were analyzed using Pearson's R correlation. Paired-samples t-test was used to evaluate significant differences of psychiatric symptoms between T1 and T2. The P value of less than 0.05 ($p < 0.05$) was considered statistically significant.

3. Results

The results of the analysis performed by Pearson coefficient correlation are shown on **Table 1**. The age of the subjects was positively correlated with Depression ($r = 0.119$, $p < 0.05$) and negatively correlated with Phobic Anxiety ($r = -0.178$, $p < 0.05$). The same variables, Depression and Phobic Anxiety, were negatively correlated with the level of education ($r = -0.231$, $r = -0.320$, $p < 0.05$) and with the dimension Somatization ($r = -0.208$, $p < 0.05$). Regarding marital status, variable Somatization was positively correlated with unmarried patients ($r = 0.141$, $p < 0.05$), while variable Phobic Anxiety was negatively correlated with unmarried women ($r = -0.105$, $p < 0.05$). Employment status encouraged a discrete mental and physical balance. Specifically, the dimensions Somatization, Phobic Anxiety and Depression were positively correlated with the variable "unemployment" ($r = 0.236$, $r = 0.218$, $r = 0.202$, $p < 0.05$).

In relation to the type of infection, the dimension Anxiety was positively correlated with patients affected with toxoplasmosis ($r = -0.236$, $p < 0.05$). This finding may explain the reaction of alertness and apprehension of pregnant women infected with *T. gondii*. In fact, the rigid patterns of therapy for long periods of time may create a mental state of Phobic Anxiety [14].

The results of the comparison between psychic variables analyzed by SCL-90 R at T1 with T2 performed using paired-sample t-test are shown on **Table 2**. We can see an improvement of the variables Anxiety and Somatization in the whole sample after the attendance at the counseling psychotherapeutic program.

4. Discussion

The psychic variables explored through SCL-90 R test are an expression of a genuine psychological distress. The levels of concern about the possible severity of the disease are high and can play a central role in one person's life, becoming a feature that negatively influences interpersonal relationships. It is generally accepted that experiences of illness during critical periods such as prenatal, perinatal and early childhood stages of life may impact on brain systems, on affective and social sphere, influencing the immediate and long-term behavior [15]. The reaction to the disease can manifest itself with obsessive behaviors, phases of depression, anxiety and agitation, according to

Table 1. Correlation by Pearson Coefficient between results of the SCL-90-R test and the characteristics of the study population (T1, 12 - 18 gestational weeks).

AGE	-0.021	-0.033	-0.078	0.119	-0.010	-0.077	-0.178	0.050	0.009
EDUCATION	-0.208	-0.166	-0.238	-0.231	-0.280	-0.300	-0.320	-0.206	-0.247
MARITAL STATUS*	0.141	-0.078	-0.072	-0.029	-0.075	0.063	-0.105	-0.032	-0.100
EMPLOYMENT STATUS**	0.236	0.266	0.179	0.202	0.254	0.245	0.218	0.003	0.002
CMV or TOXO Infection***	-0.086	-0.046	0.050	-0.005	-0.236	0.039	-0.051	0.069	0.006

Abbreviations: Somatization (SOM), Obsessive-Compulsive (OBS), Interpersonal Sensitivity (INT), Depression (DEP), Anxiety (ANX), Hostility (HOS), Phobic Anxiety (PHOB), Paranoid Ideation (PAR), and Psychoticism (PSY). *Married = 1, Unmarried = 2; **Employed = 1, Unemployed = 2; ***Toxo = 1, CMV = 2.

Table 2. Paired-samples t-test between T1 (12 - 18 gestational weeks) and T2 (after the counseling about behavioral change program).

Variables	T1		T2		t	p
	M	SD	M	SD		
SOM	8.82	6.951	6.05	5.342	2.411	0.017
OBS	6.06	6.627	4.12	5.347	1.742	ns
INT	3.24	4.445	2.31	3.681	1.228	ns
DEP	7.93	7.610	5.81	6.605	1.602	ns
ANX	6.50	6.190	4.25	5.372	2.082	0.039
HOS	3.24	3.700	2.87	3.807	0.519	ns
PHOB	1.50	3.224	1.13	2.762	0.649	ns
PAR	2.75	3.394	2.63	3.467	0.189	ns
PSY	2.84	4.475	2.77	4.660	0.081	ns

Abbreviations: Somatization (SOM), Obsessive-Compulsive (OBS), Interpersonal Sensitivity (INT), Depression (DEP), Anxiety (ANX), Hostility (HOS), Phobic Anxiety (PHOB), Paranoid Ideation (PAR), and Psychoticism (PSY), Standard Deviation (SD), not significant (ns).

the personological structure and the inner psychic world.

Our study suggests the presence of anxiety and somatization in pregnant women infected with *T. gondii* or CMV. These psychiatric symptoms could be the expression of a phase of emotional fragility with the concern of transmitting a serious disease to the unborn child [16]. The program “Counseling about behavioral change” has allowed us to create an atmosphere of trust and to understand how useful the technique of “empathic listening” was. Also, giving correct and accurate information about the disease reassures the patient and prevents negative thoughts and further concern and discomfort. Finally, creating motivation to change behavior-problem, brings out new coping strategies [17]. Despite the extensive research documenting the significance of medically unexplained somatic symptoms in primary care patients, few studies have examined somatic symptoms as a predictor of depressive and anxiety disorders among pregnant women with TORCH infection [18] [19].

5. Conclusion

Eliciting and tracking somatic symptoms during prenatal visits could potentially improve the detection of depressive and anxiety disorders in the obstetrical sector. The experience of this study allowed us to understand the importance of taking charge of pregnant women with TORCH infection. A good psychological support helps the understanding of their fears as well as their concerns for the unborn baby and can reduce or even prevent the onset of somatic symptoms. New approaches in both research and clinical medicine could reinforce the current knowledge and establish new methods of prevention strategies as well as to contribute to the development of a modern personalized medicine. In this sense, the collaboration between microbiologists, hygienists, psychologists and psychiatrists shows its validity because it is possible to get in time any symptoms about the psycho-emotional sphere in order to provide targeted care pathways [10] [20].

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