***Study of interleukins ( IL-8 , IL-17 ) and Phospholipid antibodies among agroup of aborted women infected by Cytomeglovirus in Babylon provence***

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**Abstract :-**

 Thirty four (34) women with single or more abortion having antiphospholipids antibodies, were selected as a test group as well as (15) healthy, matched age group women as a control group. Evaluation of Anti CMV, IgM and IgG, Phospholipid , IgM and IgG, were done as well as interleukin - 8 , interleukin -17, also done in clinical immunology unit in Babylon public health laboratory at the period between January and August 2013. Different types of antibodies against cytomegalovirus , IgM and IgG in a group of aborted women with or without antiphospholipid antibody assessment with some interleukins such as interleukin -8 ( IL-8) and IL-17 to monitor the immunological status of such patients . The age range group 25-34 years have 46% as a higher infected group having specific IgM antiphospholipid antibody . The middle age group is the proper age for growth activity, pregnancy as well as immunological activity rather than other age group and widely distributed of IgG antiphospholipid antibody rather than IgM. Highly significant increased in interleukins (IL-8 and Il-17) level in comparison with control and the non infected patient high low level than infected. The IgM antibody for CMV is more important than IgG and presence of both IgM and IgG among same patients need more follow up than patients with either IgM or IgG alone . Chronic CMV infection differ from acute in regarding of interleukin levels , IL-8 level shows highly significant increased among infected patient with IgG CMV antibody in comparison with control and non infected one . While IL-17 level give no significant decreased in it level among infected patients in comparison with control and also after comparison with non infected patients.

**Introduction :-**

 The test determine the presence of CMV antibodies and is routinely done in congenitally infected new born , immunocompromised patients and sexually active persons who present with mononucleosis like symptoms . (Abbas and Lichtman , 2006). Cytomegalic inclusion disease is generalized infection of infant caused by intrauterine or early post natal infection with the CMV . CMV poses an important public health problem because of its high frequency of congenital infection , which may lead to severe congenital anomalies ( Hassan , et al 2007).

 Fetal loss and abortion are responsible for significant emotional distress for couples desiring children. There are many documents which support the role of some certain asymptomatic infections such as Cytomegalovirus (CMV) in spontaneous abortion.Higher seropositivity for cytomegalovirus (CMV)in women with spontaneous abortion compared to women with normal obstetric history suggests that cytomegalovirus Plays a significant role in abortion.( Maysara , et al., 2012)

 Infant who acquire CMV during primary infection of the mother and prone to develop sever cytomegalic inclusion diseases , may be fatal or may cause neurologic sequel . Sero conversion or a significant rise in titer between acute and convalescent sera may indicate presence of a current or recent infection, Although the presence of IgM antibodies suggest current or resent infection , low levels of IgM antibodies may occasionally persist for more than 12 months after infection . (Frances , et al 2009 ) . About 1% of live births annually in the united states have congenital CMV infections , and about 5-10% of these will suffer cytomegalic inclusion . About one-third of pregnant women with primary infection transmit these viruses. Fatal damage results from reactivated maternal infections ( Hengel, et al 1998 ). Antibodies to CMV in human increase with age from about 40% in teenagers to more than 80% in these over 60 years old . Detection of viral IgM antibodies suggests a current infection . Antibody prevalence may be moderate 40 -70% in adults in high socioeconomic groups in developed countries in contrast to prevalence of 90% in children and adults in developed nations and in low socioeconomic groups ( Geo, et al 2010).

 Many infections have been found to be associated with antiphospholipid antibodies (aPL), although a pathogenic role for these antibodies has not usually been obvious except in a few isolated cases. Two types of aPL have been referred to as “autoimmune” and “infectious” types. This distinction, however, has subsequently been found not to be absolute. ( Asherson and Cervera , 2003).

***Patients and methods :-***

 Thirty four (34) women with single or more abortion having anti phospholipids antibodies, were selected as a test group as well as (15) healthy, matched age group women as a control group. Evaluation of Anti CMV, IgM and IgG, Phospholipid , IgM and IgG, were done by using manual principle and procedure of Biochick company , interleukin - 8 , interleukin -17 , also done by using manual procedure and principle of Biosource company in Babylon public health laboratory at the period between January and August 2013 in clinical immunology unit .

**Result and Discussion :-**

 The present study dealing with different types of antibodies against cytomegalovirus , IgM and IgG in a group of aborted women with or without antiphospholipid antibody . In addition assessment of some interleukins such as interleukin -8 ( IL-8) and IL-17 to monitor the immunological status of such patients in association with these categories.

**Table ( 1) Age groups distribution of IgM antiphospholipids antibody among aborted women .**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age group | Total No. | No. of positive  | Percent  | Statistic  |
| 14 -24 | 12 | 2 | 12.5 % | A |
| 25 -34 | 13 | 6 | 46 % | B |
| 35-44 | 9 | 0 | 0.0 % | C |

The table ( 1) shows the age range distribution of IgM antiphospholipid antibody . This tables shows that the age range group 25-34 years have 46% as a higher infected group having specific IgM antiphospholipid antibody , with a significant difference in comparison with other groups (14 -24 and 35 -44). This result might refers to that of the middle age group is the proper age for growth activity, pregnancy as well as immunological activity rather than other age group. Presence of IgM also might refers to acute infection or reactive immune response caused increased in phospholipid antibody.

**Table ( 2 ) Age groups distribution of IgG antiphospholipids antibody among aborted women**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age group | Total No. | No. of positive  | Percent  | Statistic  |
| 14 -24 | 12 | 6 | 50 % | A |
| 25 -34 | 13 | 5 | 38 % | A |
| 35-44 | 9 | 4 | 44 % | A |

 Table ( 2) shows that no significant difference in positive percent of aborted women having IgG antiphospholipid antibody and the age range group ( 14 -24 years) have higher percent followed by age group (35 -44 years ) . This result might refers to that highly IgG antiphospholipid among both young and adult age groups as pre exposure antibody or associated with other diseases , the antiphospholipid phenomena is present at different types of diseases such as autoimmunity and malignancy . From this result can concluding the fact that widely distributed of IgG antibody rather than IgM in comparison between antiphospholipid IgM and IgG patients.

 **Table (3) Relationship between interleukins and aborted women with Phospholipid IgM antibody and control:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Patients groups  | Total No. | IL-8 pg/ml | Il-17 pg/ml | Statistic |
| Infected  | 8 | 976.8 ± 455.3 | 949.9 ± 211.5 |  LSDIL-8 = 63.4 IL-17 = 58.7   |
| Non infected  | 26 | 705.1 ± 213.0 | 722.13± 142.6 |
| Control  | 15 | 487.7 ± 134.6 | 532.6 ± 127.8 |

The result of both interleukins IL-8 and Il-17 among aborted women with and without antiphospholipid IgM antibody shows that highly significant increased in interleukins level in comparison with control and the non infected patient high low level than infected as shown in table ( 3) .

 **Table (4) Relationship between interleukins and aborted women with Phospholipid IgG antibody and control:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Patients groups  | Total No. | IL-8 pg/ml | Il-17 pg/ml | Statistic |
| Infected  | 15 | 698.7 ± 277.2 | 1152 ± 154.0 |  LSDIL-8 = 38.41IL-17 = 25.9   |
| Non infected  | 19 | 824.6 ± 271.9 | 849.2± 170.8 |
| Control  | 15 | 487.7 ± 134.6 | 532.6 ± 127.8 |

This result might shows that chemotactic activity are more enhancement in such patients as well as increased in Th activity especially Th17 . The same result appear in IL-17 among patients with IgG antiphospholipid antibody and highly significant increased after comparison with control as shown in table ( 4) , but the result of IL-8 shows that highly significant increased in both infected and non infected patients but in low level among infected patients than non infected. This result might shows that the activity of Th cells in chronic state is more than acute and there is low activity for other inflammatory cells such as neutrophil because low chemotactic interleukin produced.

**Table ( 5) Age groups distribution of IgM anti CMV antibody among aborted women .**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age group | Total No. | No. of positive  | Percent  | Statistic  |
| 14 -24 | 12 | 2 | 12.5 % | A |
| 25 -34 | 13 | 0 | 0.0 % | B |
| 35-44 | 9 | 1 | 11.0 % | C |

**Table ( 6) Age groups distribution of IgG anti CMV antibody among aborted women .**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age group | Total No. | No. of positive  | Percent  | Statistic  |
| 14 -24 | 12 | 0 | 0.0 % | A |
| 25 -34 | 13 | 0 | 0.0 % | B |
| 35-44 | 9 | 2 | 22.0 % | C |

Table ( 5) shows that the age range group (14-24 years ) have percent (12.5%) of IgM CMV antibody as a higher percent than other age groups. This result might be show that few percent of aborted women mentioned in present study give an antibody against cytomegalovirus , in two types IgM and IgG but the same group having no IgG antibody as mentioned in table (6) , the age range 35-44 have more percent ( 22.0%) of IgG CMV antibody , and among this group there is one patient having both antibody type IgM and IgG . The IgM antibody for CMV is more important than IgG and presence of both IgM and IgG among same patients need more follow up than patients with either IgM or IgG.

 Infected patients with CMV at acute stage or in association with presence of IgM antiphospholipid antibody shows that highly significant increased in both interleukins ( IL-8 and IL-17) in comparison with control , at concentration mean ± S.D (1335.8 ± 295.2 , 733.6 ± 194.1 and 487.7 ± 134.6) for infected , non infected and control respectively with LSD value ( IL-8 = 16.24 , IL-17 =34.9) , while infected patients shows that no significant decreased in IL-17 level in comparison with non infected , it mean that the phospholipid antibody more affected the IL-17 level than CMV IgM antibody. As shown in figure ( 1) among 3 infected patients , 31 non infected and 15 for control .

**Figure (1) Relationship between interleukins and aborted women with CMV IgM antibody and control**

 This result is contituent with other study such as Nielson , et al., (1988) who stated that fhe presence of CMV-specific Immunoglobulin M (IgM) may not be indicative of primary infection, since it is also produced during reactivation and re infection.

It has been reported that the risk of fetal damage is greater if the primary infection occurs during the first trimester of pregnancy (Stango , et al., 1986 ). Primary CMV infection in an individual can be detected by demonstration of CMV specific IgM antibody (Balasubramanium ,et al., 1994). CMV specific IgM antibody was detected in (15.7% ) of all pregnant women tested indicating the substantial prevalence of infection in local population (Maysara , et al., 2012).

Cytomegalovirus (CMV) infection during pregnancy is more complex than other infections, due to virus reactivation during the child bearing age and be transmitted to the fetus in spite of maternal immunity. CMV infection is endemic in Iraq in (2002);the prevalence rates of human cytomegalovirus IgM and IgG in non pregnant women have been reported to be 1% and 84% respectively ,and 2.5% and 90% in pregnant women (Alwan , 2011).

 Chronic CMV infection differ from acute in regarding of interleukin levels and the result as shown in figure ( 2) refers to that IL-8 level shows highly significant increased among infected patient with IgG CMV antibody in comparison with control and non infected one . While IL-17 level give no significant decreased in it level among infected patients in comparison with control and also after comparison with non infected patients. at concentration mean ± S.D of IL-8 (1335.8 ± 295.2 , 733.6 ±194.1 and 487.7 ± 134.6) respectively for infected , non infected and control . And IL-17 ( 502.82 ± 355.55 , 702.55± 124.19 and 532.6 ± 127.8) as shown in figure (2) among 2 infected patients , 32 non infected and 15 control respectively .

**Figure (2) Relationship between interleukins and aborted women with CMV IgG antibody and control**

 Zhao ,et al., ( 2011) who mentioned that the T helper (Th)17 response plays an important role in murine cytomegalovirus (MCMV) interstitial pneumonia. The levels of IL-17 in the serum were significantly higher in MCMV-infected mice versus not-infected mice. IL-17 production increases locally and systemically during MCMV interstitial pneumonia. Neutralization of IL-17 significantly suppressed lung inflammation at day14 as assessed by histology. These findings suggest that IL-17 is important in the pathology of MCMV interstitial pneumonia.

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