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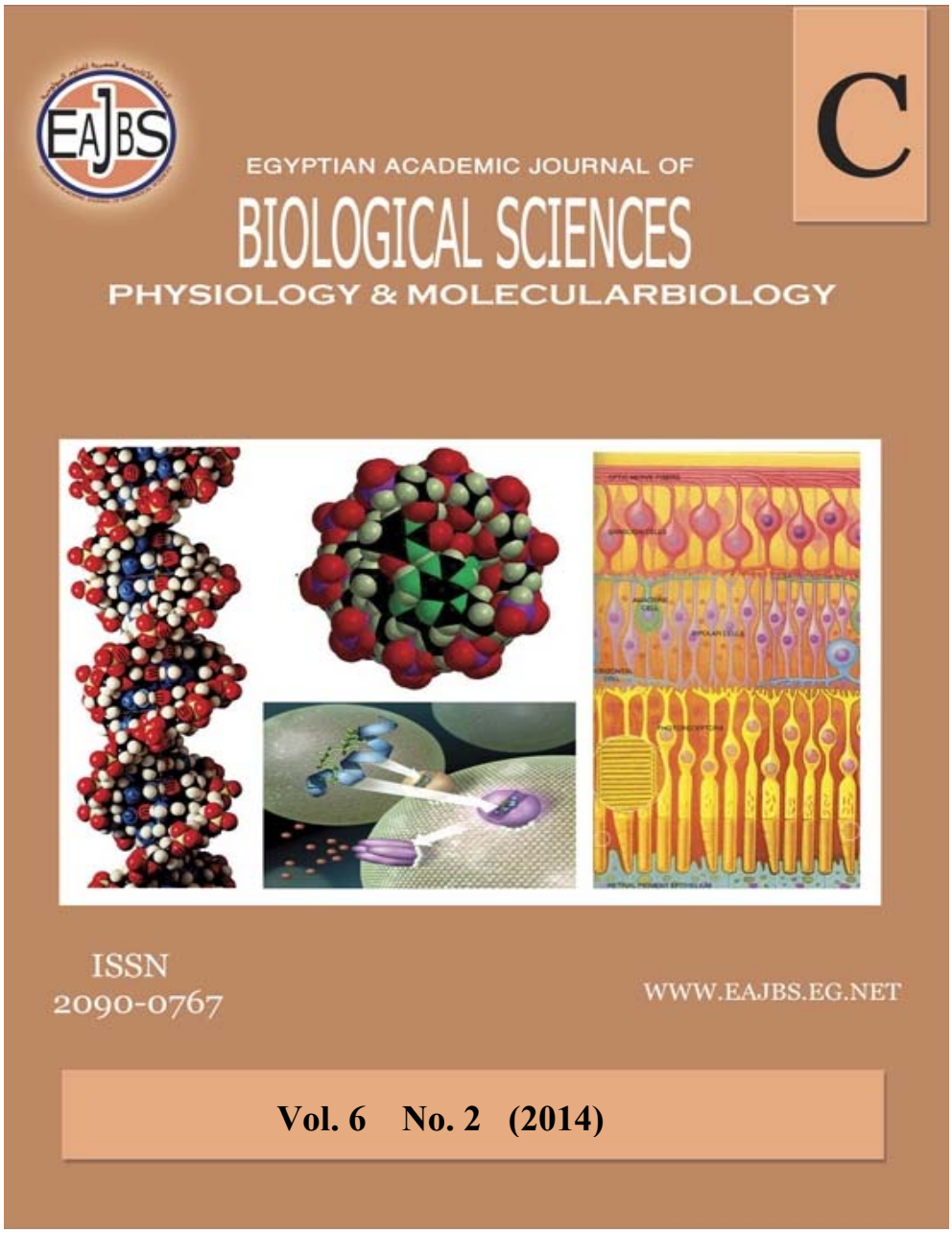

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Frequency of Tuberculous Lymphadenitis among Sudanese Pediatric patients

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ABSTRACT

Background: Tuberculosis (TB) is one of the major health challenges in many developing countries and in Sudan in particular. The aim of this study was to screen pediatric patients suspected with lymph Node (LN) TB for the presence of tuberculosis.

Methodology: This study investigated retrospectively 42 LN biopsies taken from pediatric patients for evidences indicating the presence of *Mycobacterium Tuberculosis (MT).* Hematoxylin and Eosin (HE), Zielnelson (ZN), Immunohistochemistry (IHC) and Polymerase Chain Reaction (PCR) techniques were used for diagnosis.

Results: For HE giant cell granuloma and caseation were evidenced in 33/42(78.6%), since epitheloid granuloma was evidenced in 9/42(21.4%). Positive ZN, IHC and PCR were indicated in 1/42(2.4%), 33/42 (78.6%) and 33/42(78.6%), respectively.

Conclusion: pediatric TB is still prevalent in some parts of Sudan. More effective health strategies are urgently needed in Sudan, particularly in eastern Sudan to control the disease.

INTRODUCTION

Tuberculosis (TB) is second only to Human immunodeficiency virus (HIV) as the greatest killer worldwide due to a single infectious agent (Kazemnejad, *et al*. 2014). In 2012, 8.6 million people fell ill with TB and 1.3 million died from TB. Over 95% of TB deaths occur in low- and middle-income countries, and it is among the top three causes of death for women aged 15 to 44. In 2012, an estimated 530 000 children became ill with TB and 74 000 HIV-negative children died of TB (WHO, 2013). Lymphadenopathy is the disease of the lymph nodes that rendering them abnormal in size and consistency (Nield and Kamat, 2004). Lymphadenopathy is a relatively common condition in the pediatric age group (Hanif, *et al*. 2009). The etiologies are multiple; and various pathological conditions should be considered in the differential diagnosis of a child with chronic lymphadenopathy. TB infection is the most common trigger for lymph nodes enlargement. Tuberculosis lymphadenitis (historically referred to as scrofula) is the commonest form of extra pulmonary TB recorded in children from TB-endemic areas, present in 8–10% of children diagnosed with TB in India and South African (Reddy, *et al*. 2002; Marais, *et al*. 2006).

In developing countries there is still difficulty to differentiate tuberculosis lymphadenitis from other condition that cause lymph node enlargement (Bayazıt *et al*. 2004). The aim of this study was to screen pediatrics patients with lymphadenopathy for the presence of tuberculosis using different diagnostic technique.

MATERIALS AND METHODS

This retrospective study was carried out at the Histopathology Department of the National Laboratory in Sudan, including samples referred to the laboratory during the period from 2008 to 2011. Tissue samples were retrieved from 161 lymph node biopsies among whom 42/161 (26%) were pediatric patients presenting with lymphadenopathy, and the diagnosis of tuberculosis was confirmed through various specific tests including H&E for histopathology, Zielnelson (ZN), Immunohistochemistry (IHC) and Polymerase Chain Reaction (PCR) techniques. The clinical data of the patients were retrieved from laboratory records.

RESULTS

This study investigated retrospectively 42 LN biopsies taken from pediatric patients for histopathological evidences indicating the presence of *MBT*. The age range was from 4 to 18 years with a mean age of 11years, the male female ratio was equal. Most biopsies were from cervical LN (64.3%), followed by axillary LN(14.3%) and mediastinal LN, mesenteric LN, lingual LN, sub-mandibular LN, constituting 7%,4.8%, 4.8%,4.8: respectively, as indicated in Fig.1. HE, ZN, IHC and PCR techniques were used for diagnosis. For HE giant cell granuloma and caseation were evidenced in 33/42(78.6%), since epitheloid granuloma was evidenced in 9/42(21.4%). Positive ZN, IHC and PCR were indicated in 1/42(2.4%), 33/42 (78.6%) and 33/42(78.6%), respectively. Of the 21 males 19/21 (90.5%) were found positive, hence, the positive females were 14/21 (66.7%). In conclusion the risk of lyphadenopathy associated with LN tuberculosis was tremendously significant (P <0.0001). More effective health strategies are urgently needed in Sudan, particularly in eastern Sudan to control the disease.

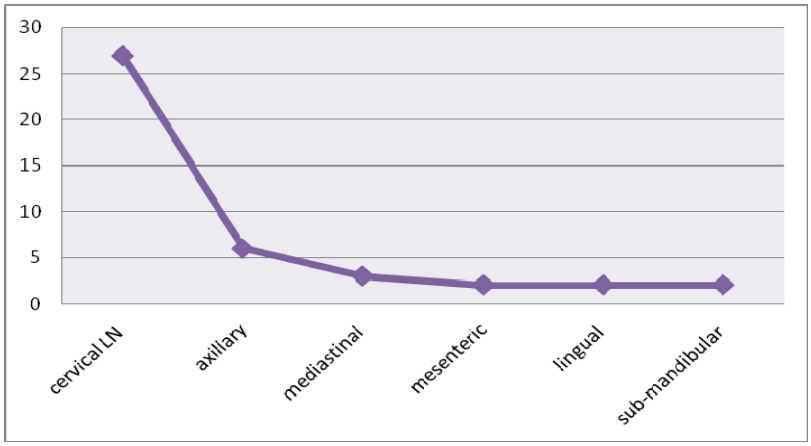

Fig. 1: Description of the study population by Lymph node site

DISCUSSION

Sudan is a large country with miscellaneous population and history of civil conflict. Poverty levels are high with poor health delivery system. The country has a high burden of tuberculosis (TB) with an estimated 50,000 incident cases during 2009, when the estimated prevalence was 209 cases per 100,000 of the population (Ghada, *et al*. 2011). Incidence and prevalence of lymph node tuberculosis in Sudan is poorly documented. In 1992, Kheiry *et al*. drew attention to the fact that there were an

increasing number of cases in Khartoum (Kheiry and Ahmed, 1992).

The findings of this study showing high frequency of pediatric Tuberculous lymphadenitis among patients attending with lymph node associated TB. In the present study out of (n=161) enlarged lymph node, 42 (26%) were pediatrics, the remaining were adult, these findings similar to previously published study from same country carried in 2003 by Aljafari *et al*. (2004). In a study from Sudan, a total of 670 patients were registered at Kassala hospital with clinical, laboratory and radiological evidence proven TB. Pulmonary TB accounted for 73.4% while extra-pulmonary TB was reported in 26.6% of all TB patients (Tajeldin, *et al*. 2012).

In this study 42 LN biopsies from pediatric patients was investigated retrospectively, using ZN, IHC and PCR. The age range was from 4 to 18 years. The majority of biopsies were from cervical LN (64.3%), these findings are in concordance with previously published results from this country carried by Aljafari *et al*. (2004) and study carried in USA by Talavera and Miranda (2001). In Yemen Hussain *et al*. (2001) reported similar results to ours.

PCR using IS6110 oligonucleotides and IHC using anti 38 KD are the most recently applied methods in the diagnosis of tuberculous lymphadenitis (Baek, *et al*. 2000; Goel, *et al*. 2001). It proved to be highly sensitive and specific as was clearly demonstrated by this study.

Accordingly our PCR and IHC result showed higher sensitivity and specificity than Z.N stain in detection of lymph node tuberculosis, this finding such finding have reported by Juan Rodrguez *et al*. (2012) and Tehmina Mustafa *et al*. (2006) also their results, combined with findings from a previous study carried by Honore, *et al*. (2001).

Lymphadenopathy due to tuberculosis was found in (78.6%) of Sudanese pediatric patients in this study using PCR and IHC which is much over than the report in 2012 from the same country by Bilal and Elshibly (2012) who reported a rate of (10%), and even much over than report of similar study from Greece by Papadopouli *et al*. (2009) who reported (12%) in 2009. This may be attributed to the low specificity and sensitivity of other technique and strategies for the diagnosis of the lymphadenopathy, that may have a false negative rate of would have been more yielding if combined with PCR, a costly tool of diagnosis in a developing country (Goel, *et al*. 2001).

In conclusion the risk of lymphadenopathy associated with LN tuberculosis was tremendously significant (P <0.0001). More effective health strategies are urgently needed in Sudan, since, TB continues to be an important public health problem in Sudan, particularly among younger population.

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ARABIC SUMMARY

تردد مرض السل فى العقد الليمفاوية بين مرضى الأطفال السودانيين

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خلفية: مرض السل هو واحد من التحديات الصحية الرئيسية في العديد من البلدان النامية بصورة عامة ولا سيما السودان على وجه الخصوص. كان الهدف من هذه الدراسة هو الكشف عن وجود مرض السل فى الأطفال المرضى الذين لديهم تضخم فى العقد الليمفاوية.

المنهجية: كانت هذه الدراسة دراسة ارتجاعية للكشف على مرض السل للأطفال الذين لديهم تضخم فى العقد الليمفاوية. تم إستخدام صبغى الهيماتوكسلين والايوسن بالإضافة الى الصبغة المقاومة للأحماض، كيمياء الانسجة المناعية و تفاعل البوليميريز المتسلسل للتحقق من وجود مرض السل.

النتائج: بالنسبة لصبغة الهيماتوكسلين والأيوسين استخدم وجود الخلايا العملاقة والتجبن كدليل قوى لوجود مرض السل فى العقد الليمفاوية، واتضح وجود مرض السل فى عدد ٤٢/٣٣(٧٨.٦%) من العينات. كانت النتائج الموجبة لكل من الصبغة المقاومة للامراض، كيمياء الانسجة المناعية، تفاعل البوليميريز المتسلسل هى ٤٢/٩(٢.٤%)، ٤٢/٣٣(٧٨.٦) و ٤٢/٣٣(٧٨.٦%) على التوالى.

الأستنتاج: مرض السل فى الأطفال مازل سائداً فى بعض مناطق السودان لاسيما فى شرق السودان على وجه الخصوص.لذا يجب أن تكون هنالك استراتيجيات صحية أكثر فعالية للسيطره على المرض.