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LEGIONNAIRES' DISEASE IN THE RENAL TRANSPLANT UNIT OF "HOSPITAL DAS CLINICAS, FMUSP". DURING A FIVE YEAR PERIOD (1988-1993)

Neusa Augusta de Oliveira MAZIERI (1), Cid Vieira Franco de GODOY (2), Solange Figueiredo ALVES (3), Dahir Ramos de ANDRADE (4), Ana Sara S. LEVIN (5) & Ana Cristina HABLITZEL (6).

SUMMARY

Several reports have related *Legionella pneumophila* with pneumonia in renal transplant patients, however this association has not been systematically documented in Brazil. Therefore this paper reports the incidence, by serologycal assays, of *Legionella pneumophila* serogroup 1 in these patients during a five year period. For this purpose sera from blood samples of 70 hospitalized patients with pneumonia from the Renal Transplant Unit of Hospital das Clinicas, FMUSP collected at the acute and convalescent phase of infection were submitted to indirect immunofluorescence assay (IFA) to demonstrate anti-*Legionella pneumophila* serogroup 1 antibodies. Of these 70 patients studied during the period of 1988 to 1993, 18 (25.71%) had significant rises in specific antibody titers for *Legionella pneumophila* serogroup 1. Incidence was interrupted following Hospital water decontamination procedures, with recurrence of infections after treatment interruption. In this study, the high susceptibility (25.71%) of immunodepressed renal transplant patients to *Legionella pneumophila* serogroup 1 nosocomial infections is documented. The importance of the implementation and maintenance of water decontamination measures for prophylaxis of the infection is also clearly evident.

KEYWORDS: Legionnaires' disease; Renal transplant unit.

INTRODUCTION

The association of *Legionella pneumophila* with pulmonary infections in patients submitted to renal transplantations has been reported by several investigators (AGUILAR et al. [1]; AMPEL & WING [2]; BOCK et al. [4]; FOSTER et al. [12]; HALEY et al. [16]; MARSHALL et al. [21]; TOBIN et al. [35]). In Brazil, publications regarding *Legionella sp.* are related to clinical descriptions (BETHLEM & GUSMÃO [3]; DE PAULA et al. [8].; PEREIRA E SILVA [31]; PORTO et al. [34]), serological survey in blood donors and intensive care units staff (VERONESI [36]), isolation from a community acquired case (PEREIRA GOMES et al. [33]), renal transplant unit (LEVIN et al. [19], MAZIERI [22]; MAZIERI et al. [25]) and finally *Legionella spp* isolation from nosocomial and industrial environment (PELLIZARI [30]). The positive results of these initial studies in this country motivated

(1) Farmacêutica - Bioquímica, Laboratório de Investigação Médica (LIM-54). Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP). São Paulo, Brazil.
(2) Prof. Resp. Disc. Patol. Clínica, Departamento de Patologia da FMUSP, LIM-54 e Instituto de Medicina Tropical de São Paulo, S. P., Brazil.
(3) FMUSP, LIM-54, HC-FMUSP.
(4) Diretor Clínico do Dep. de Moléstias Infecciosas e Parasitárias do HC-FMUSP e chefe do LIM-54, Bacteriologia.
(5) Membro da Comissão de Infecções do ICHC-FMUSP.
(6) Prof. Adj. Microbiologia - Universidade de Mogi das Cruzes.
Endereço para correspondência: Neusa Augusta de Oliveira Mazieri - Rua Fernão Dias 128, apto. 191 - Pinheiros, São Paulo, Brazil. CEP 05427-000.

the present study with immunodeppressed patients, specifically with patients in the renal transplant unit of Hospital das Clínicas, Faculdade de Medicina, of the University of São Paulo.

METHODS

From a total number of 250 patients with pulmonary infections in Hospital das Clínicas, submitted to specific laboratory tests for legionellosis, during the period of July, 1988 to July, 1993, 70 were renal transplant subjects.

Antibody testing for *Legionella pneumophilia* serogroup 1 were carried out by the indirect immunofluorescence test in paired sera collected in the acute and convalescent phase of the disease, using the heat-inactivated *Legionella pneumophila* serogroup 1 (Philadelphia) strain and anti-human polyvalent immunoglobulins (IgA, IgM and IgG) conjugate (MAZIERI [22]; WILKINSON [37]). Recommendations from Centers for Disease Control (WILKINSON [37]) were followed to interpret results: a fourfold antibody titer rise in paired sera or significant titer equal to or above 256 when accompanied by agent isolation.

RESULTS

Of the 70 hospitalized patients studied in the Renal

TABLE 1

Annual distribution of incidence of Legionnaires'Disease (LD) at the Renal Transplant Unit (RTU) and pulmonary infections at RTU and other units of Hospital das Clínicas da Faculdade de Medicina, University of São Paulo (HC-FMUSP).

Year July/July	cases of pneumonia HC-FMUSP	cases of pneumonia RTU	incidence of LD (RTU)
1988/1989	26	0	0 (0%)
1989/1990	53	29	9 (31.03%)
1990/1991	63	19	2 (10.52%)
1991/1992	78	17	7 (41.17%)
1992/1993	30	5	0 (0%)

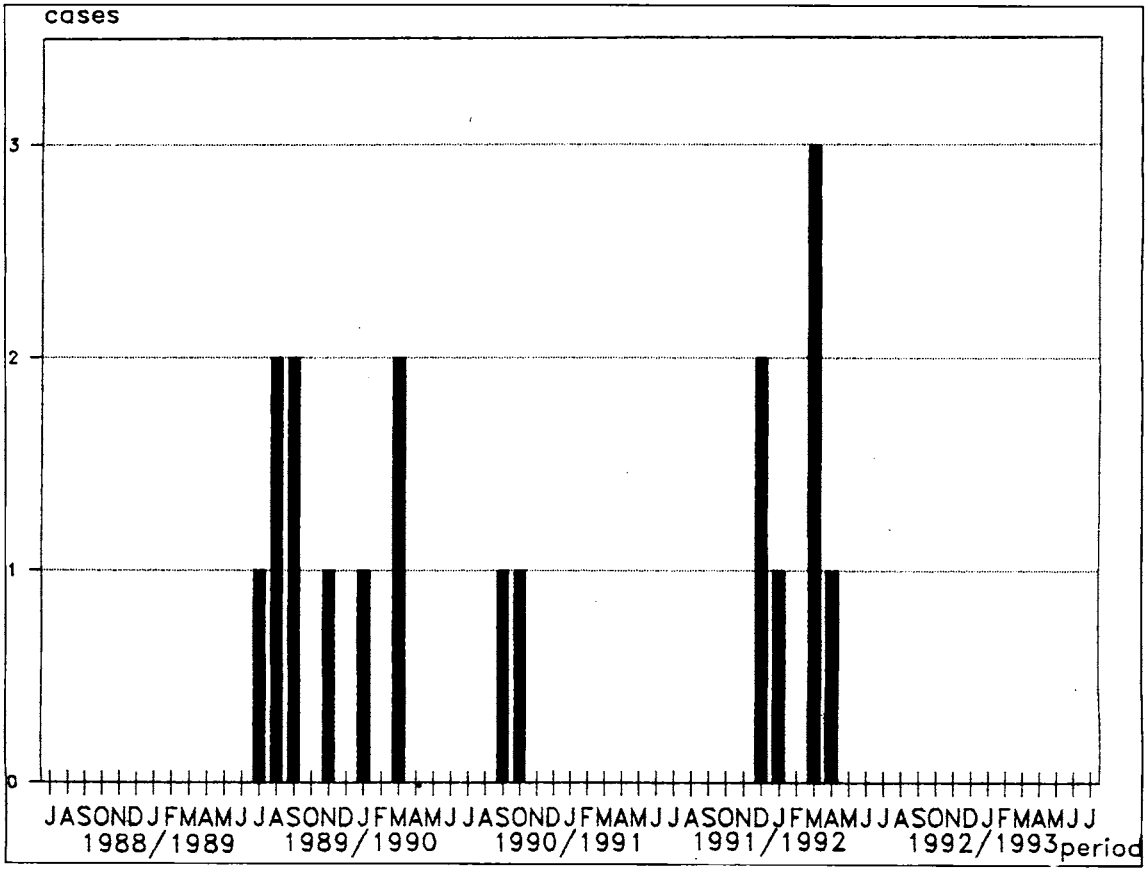

Figure 1 - Monthly distribution of cases of Legionnaires' Disease at the Renal Transplant Unit (RTU), Hospital das Clínicas da Faculdade de Medicina, University of São Paulo (HC-FMUSP), during July 1988 to July 1993.

Transplant Unit (RTU) during the period of July 1988 to July 1993 with pulmonary infections, 18 (25.71%) presented significant specific sera antibody titers to *Legionella pneumophila* serogroup 1. The incidence, monthly and annual distribution of the cases are shown in table 1 and figures 1 and 2.

DISCUSSION

The precise incidence of legionellosis in the population has not been yet determined (W. H. O., [38]). Preventive measures are recommended to avoid legionella contamination in areas where patients may be more susceptible (ENGLAND & FRASER [11]; GARBE et al. [13], KIRBY et al. [18], LOWRY & TOMPKINS [20]; MUDER et al. [28]; NEIL et al. [29]) such as immunodepressed patients due to illness, age or therapy (radiation therapy, anticancer or immunodepressive drugs). Fatality rates of Legionnaires'Disease are more elevated in these nosocomial cases (30-50%) than in community-acquired cases. This fact is thoroughly comprehensible, for in Hospitals, besides the contamination source there are high risk subjects to acquire the infection. In hospitalized populations, that are exposed to the agent, predective values for attack rate and mortality are high (W. H. O. [38]).

Water system (mainly heated water) are common sources of infection: these systems are usually of major complexity, mainly in hospital edifications that were enlarged or modified. The site of legionella propagation may be water ontlets such as faucets (BOLLIN et al. [5]), showers (DENNIS et al. [9], TOBIN et al. [35]), bathtubs (BOLLIN et al. [5]), cooling towers (DONDERO et al. [10]; KLAUCHE et al. [17]; MITCHELL et al. [27]), condensed water collector trays from airconditioning systems (LEVIN et al [19]), plumbing system shock absorbers (MEMISH et al. [26]), etc.

When the present study was initiated, following isolation of the agent on January, 1988 (PEREIRA GOMES et al. [33]) the association of the importance of legionella in the immunodepressed was not yet known.

A total of 26 cases were initially received in our laboratory as legionellosis suspects from several wards of the Hospital das Clinicas da Faculdade de Medicina

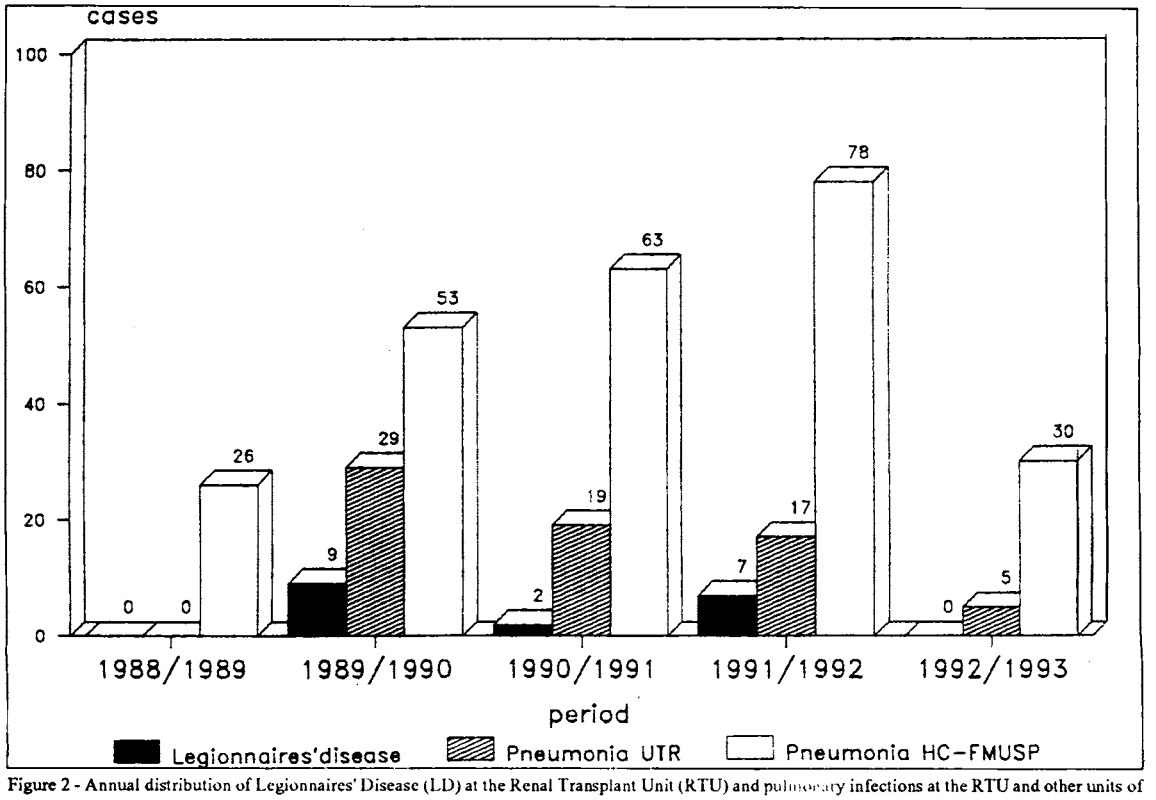

Figure 2 - Annual distribution of Legionnaires' Disease (LD) at the Renal Transplant Unit (RTU) and pulmonary infections at the RTU and other units of Hospital das Clinicas, University of São Paulo (HC-FMUSP).

USP, none proceeding however from the Renal Transplant Unit.

As a consequence of the divulgation of the role of Legionnaires' Disease in pneumonias in our country, through papers presented in several Medical Meetings: Brazilian Congress of Pneumology and Tisiology (Curitiba, 1988) [32], Brazilian Congress of Clinical Pathology (Rio de Janeiro, 1989) [25] and the Scientific Meeting of Tropical Medicine Institute of São Paulo (São Paulo, 1989) [14, 23, 24] a consensus of the application of laboratory procedures for diagnostic elucidation was accepted by our Medical Community.

Biological specimens from pneumonia patients in the Renal Transplant Unit of Hospital das Clinicas began arriving to our laboratory and in the following year (July 1989 to July 1990) of the twenty nine patients with pneumonia belonging to this Unit, 9 (31.03%) were diagnosed by laboratory procedures as Legionnaires' Disease.

Decontamination measures in the hospital water system were introduced, by hyperchloration (6-10 ppm) and heating (80 C) as described by LEVIN et al. [19].

At this time, microbiological analyses were performed in the hospital water system, with recovery of *Legionella pneumophila* serogroup 1 from the condensed water collection tray of the air conditioning system by LEVIN et al. [19] and from the water reservoir and the residue of the electric boiler, by PELLIZARI [30].

Five months following the first decontamination (in April 1990) of the hospital water system, 2 new cases of Legionellosis were diagnosed (September and October, 1990). A new decontamination by hyperchloration (6-10 ppm) was conducted and repeated after a period of five months. As a result of these procedures a period of 12 months prevailed without new cases of legionellosis. From December 1991 to April 1992, 7 new cases of the infection with pneumonia were diagnosed, and three among these had irrefutable evidence of hospital acquired legionellosis (*Legionella pneumophila* serogroup 1).

Prophylactyc procedures were performed continuously with five months intervals by hyperchloration (10 ppm) with no further legionellosis to this date at the Hospital das Clínicas.

Of the total of 70 patients with pneumonia from the Renal Transplant Unit of Hospital das Clínicas, 18 (25.71%) had laboratory diagnosis of legionellosis in a five year period (Figure 2).

Considering the low number of cases from a statystical point of view, Legionnaires' Disease incidence according to season or months of the year was not applicable to statistical evaluation but intervals between infection were clearly related to decontamination procedures. Following the nosocomial outbreak at Hospital das Clinicas from December 1991 to April 1992, it was evident that control measures were extremely necessary for an active surveillance of the disease in the exposed population, with good results to this date of the implementation of decontamination procedures.

World literature has references to surveillance of infection sources determining as causes of legionellosis outbreaks, the failure to implement control measures, descontinuation or interruption of these procedures, demonstrating the importance of monitoring water quality systematically (W.H.O.[38]). Once water treatment is introduced, it must necessarily be continuous, as bacteria reappearance is common with possibility of manifestation of clinical disease (BORNSTEIN et al. [6]; COLVILLE et al. [7]; GROOTHUIS et al. [15]; KLAUCKE et al.[17]).

CONCLUSIONS

- In the patient group included in this study, high susceptibility (25.71%) to nosocomial infection by *Legionella pneumophila* serogroup 1 of this immunodepressed renal transplant population was documented.
- The results of this study and the incidence distributions recorded support the importance of microbiological surveillance as water reservoirs and nosocomial water systems and the maintenance of continuous measures to minimize legionellosis propagation.

RESUMO

Doença dos legionários na Unidade de Transplante Renal (UTR) do Hospital das Clínicas FMUSP, no período de 1988 a 1993.

Embora vários trabalhos tem mostrado a presença de *Legionella pneumophila* associado a pneumopatias infecciosas em transplantados renais, tal associação não fora antes realizado de maneira sistemática no Brasil. Os autores julgaram oportuno a determinação

da incidência por comprovação sorológica da *Legionella pneumophila* sorogrupo 1 em transplantados renais num período de 5 anos.

Para tanto amostras de soros de 70 pacientes com pneumopatia infecciosa internados na UTR do HC-FMUSP, colhidos na fase aguda e convalescente da infecção, foram submetidas à reação de imunofluorescência indireta para pesquisa de anticorpos anti-*Legionella pneumophila* sorogrupo 1.

Dos 70 pacientes transplantados renais com pneumopatia infecciosa estudados no período de 1988 a 1993, 18 (25.71%) apresentaram amostras de soros com aumento significante de títulos de anticorpos específicos para *Legionella pneumophilia* sorogrupo 1.

A distribuição da incidência dos casos foi interrompida após medidas de descontaminação da água do nosocômio, com reincidência após a interrupção deste tratamento.

Verificaram os autores com os pacientes incluídos neste estudo a elevada suscetibilidade (25,71%) dos imunedeprimidos transplantados renais às infecções nosocomiais por *Legionella pneumophila* sorogrupo 1. Ressaltam ainda, a importância na implementação e manutenção de medidas de descontaminação da água para a profilaxia da infecção.

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