AIN SHAMS UNIVERSITY
INSTITUTE OF POSTGRADUATE
CHILDHOOD STUDIES
MEDICAL DEPARTMENT

IMMUNOGLOBULINS PATTERN IN CHILDREN SUFFERING FROM CROUP

Thesis

Submitted for Partial Fulfillment
of Ph. D. Degree in
Paediatrics

By
Manal Mohsen
(M.B., B.Ch. & M.Sc.)

Under Supervision of

Prof. Dr.
Esaad Kallaf
Professor and Chief of Paediatric Department at Al-Mataria Teaching Hospital

Dr.
Eman El-Achmawy
Assistant Professor in Paediatrics at the National Center for Researches

Dr. **Magdy Karam El-Din**
Lecturer in the Medical Department at the Institute of Postgraduate Childhood Studies, Ain Shams University

FACULTY OF MEDICINE
AIN-SHAMS UNIVERSITY
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Abstract

This thesis aimed to assess the relation between changes in immunoglobulins concentrations and the croup in children. In addition the relation between the age of the patients and the socioeconomic status with the incidence of croup.

Fifty-three children constituted the material of the study. These children were visiting Mataria Teaching Hospital, between March 1994 and December 1996. Thirty-four children were suffering from croup. Nineteen were healthy children and free from any respiratory tract infections forming the control group. The children age varied from one and half year up to twelve years old. Sex discrimination was not considered as a condition.

History and clinical examinations were done to diagnose croup in children. Serum and salivary samples were taken from the croup children and the control group to determine the level of serum IgA, IgG and IgM and also the level of salivary IgA.

Results of this study showed significant rise of serum immunoglobulins A, G and non-significant rise of serum immunoglobulin M because it is a short lasting immunoglobulin. The rise in serum immunoglobulins A, G and M was age dependent with wide individual variations. Low level of parental education, breast feeding less than 18 months, exposure to smoke fumes and to sudden change in weather were associated with increased incidence of croup.

Key Words:

Paediatrics-Respiratory system-Larynx-Croup-Immunoglobulin.

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To My Husband

Daughter and Son

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LIST OF ABBREVIATIONS

CPS	: Capsular polysaccharide.
Hib	: Haemophilus influenzae type b.
IgA	: Immunoglobulin A.
IgG	: Immunoglobulin G.
IgM	: Immunoglobulin M.

Contents

INTRODUCTION

INTRODUCTION

The term croup includes a group of acute infectious or allergic conditions characterized by a peculiar brassy (croupy) cough due to varying degrees of laryngeal obstruction. Epiglottitis represents the most serious disease among croup patients. It may be accompanied by inspiratory stridor, hoarseness, and signs of respiratory distress. Severe forms of croup threaten patients lives and urgent treatment is usually indicated.

In up to 40% of children below 5 years of age and with epiglottitis - Haemophilus influenzae type b (Hib) was the cause **(Gilbert et al., 1990 and Takala and Clements, 1992)**. Epiglottitis is the second most serious disease - after meningitis - caused by Haemophilus influenzae type b **(Turk, 1984)**. Hib infection is transmitted most commonly via droplets followed by oropharyngeal and nasopharyngeal colonization **(Beachey, 1981)**. The invasion by Hib bacteria was attributed to respiratory epithelial damage and slowed mucocillary clearance usually following viral infections and exposure to cigarette smoking **(Wilson et al., 1992)**.

When the diagnosis of croup is probable on the clinical grounds, direct viewing of the epiglottis may be indicated. This maneuver should be deferred in seriously ill children until complete cardiorespiratory support is available. Laryngoscopy is allowed only when the appropriate equipments and personnel are present to control the airway and eventually provide ventilatory assistance. Lateral roentgenography of the nasopharynx and upper airway are indicated for cases in which foreign body inhalation or retropharyngeal abscess is suspected. The serum antibody titre against Hib can be estimated as it rises after epiglottitis.

The changes in immunoglobulins concentration induced by croup of viral, bacterial or other aetiologic origin during infancy and childhood have been an interesting subject for investigators over the late one or two decades. The serum antibody responses to the capsular polysaccharide (CPS) of Hemophilus influenzae type b bacteria and to the non-capsular antigens **(Sly et al., 1988)** showed increases in all three antibody classes (IgG, IgM and IgA) in both epiglottitis and meningitis cases **(Whisnant et al., 1976)**. While some authors **(Norden et al., 1976 and Rosales et al., 1984)** did not find any antibody response in children below 18 months old, others **(Claesson et al., 1987 and Trollfors et al., 1992)** recorded a transient IgM response. Serum antibody concentrations detectable at presentation of children with epiglottitis significantly rose by 3 weeks **(Sly et al., 1988)**.

The relation between croup and epidemiological variables in children has been studied in many centers **(Istre et al., 1985 and Makela et al., 1992)**. Literature has pointed out the peak age incidence at around 3 years, the common preceding viral infection and the high susceptibility with paternal smoking, low family income, nursery attendance and most important short duration of breast feeding.

AIM OF WORK

AIM OF WORK

This study aims to assess the relation between changes in immunoglobulins concentrations and the croup in children. The relationship between the serum antibody responses and the age of the child with croup will be evaluated. In addition, the socioeconomic status of children suffering from croup will be assessed to find out any influence of the social standard on the frequency of the condition.

Questions intended to be answered are:

- ★ Is there a relation between croup and immunoglobulins serum titres?
- ★ Does the change in serum immunoglobulins depend on the age of the children with croup?
- ★ Has croup a prevalent frequency in a specific socioeconomic level?

REVIEW OF LITERATURE

- Definition of Croup
- Classification
- Epidemiology
- Aetiology
- Clinical Aspects
- Investigations
- Management
- Antibody Titres in Croup Children

REVIEW OF LITERATURE

Definition:

Croup is a generic term including a heterogeneous group of relatively acute infectious or allergic conditions characterized by a peculiar brassy (croupy) cough due to varying degree of laryngeal obstruction. It may be accompanied by inspiratory stridor, hoarseness, and signs of respiratory distress. It can threaten patient's life **(Stern, 1992 ; Cauted from Nelson Textbook of Pe;diatrics)**.

Classification:

After Nelson (1992):

I- Infectious croup:

1. Viral agents account for nearly all croup except that associated with diphtheria, bacterial tracheitis, and acute epiglottitis. The parainfluenza viruses account for approximately three quarters of all cases, with the adenoviruses, respiratory syncytial, influenza and measles viruses causing most of the remaining cases for which a viral agent can be identified.
2. Acute epiglottitis is almost always caused by Haemophilus influenzae type b. The group A streptococcus, the pneumococcus and the staphylococcus are occasionally implicated.
3. Mycoplasma pneumonia was recovered from 3.6% of patients who had croup.
4. Diphtheritic croup. Symptoms develop more slowly, although respiratory obstruction may occur suddenly.

Pharyngeal examination reveals the typical gray-white membrane.

5. Measles croup almost always coincides with the full manifestations of systemic disease, and the course may be fulminant.

6. Herpes simplex virus type I is reported by **Inglis (1993)** as a rare cause of prolonged or atypical croup.

II- Non-Infectious croup

1. Aspiration of a foreign body causes sudden onset of respiratory obstruction. The child is generally 6 months to 2 years of age. Chocking cough occurs suddenly, usually without signs of inflammation.

2. Retropharygneal abscess may also present as respiratory obstruction. Palpation of the posterior pharyngeal wall usually reveals a fluctuant mass. Roentgenographic examination of the upper airway and chest is essential in evaluating these possibilities.

3. Extrinsic compression of the airway, such as a hematoma from trauma and intraluminal obstruction from masses as cysts or tumours present as respiratory obstruction and roentgenographies are needed to evaluate this condition.

4. Croup is also occasionally associated with angioedema of the subglottic areas as part of anaphylaxis and generalized allergic reactions, edema following endotracheal intubation for anaesthesia or respiratory

failure, hypocalcemic tetany, infectious mononucleosis, trauma, tumours, or malformations of larynx. A croupy cough may be an early sign of asthma.

5. Bilateral vocal cord paralysis and psychogenic laryngospasm are considered by **Lindemann (1993)** as additional causes for croup.

Epidemiology:

Viral croup is the most common form of upper airway obstruction in children 3 months to 5 years of age. Viral croup typically presents in the cold season of the year **(Nelson, 1992).**

In **1994, Knott et al.,** reported that parainfluenza viruses are the major cause of viral croup but they also produce a spectrum of diseases ranging from mild upper respiratory tract infection to bronchitis and pneumonia. Parainfluenza viruses have a striking epidemiologic pattern and show seasonal variation in their incidence. Parainfluenza virus type 1 occurs in the fall season; while Parainfluenza virus type 2 is less predictable; and Parainfluenza virus type 3 appears yearly with peak activity in spring or summer.

Epiglottitis has been reported by **Turk in 1984** as the second most common clinical manifestation of Hib disease; it comes next in frequency to meningitis.

Although the incidence of Hib disease was often higher among blacks than others, the race was not a determinant

when the socioeconomic factors were controlled for **Cochi et al., 1986**. Sex distribution insistently shows a male predominance in literature **(Gilbert et al., 1990 and Takala and Clements, 1992)**.

The peak incidence of the age of patients with epiglottitis due to Hib disease occurs at 2.5 to 3 years **(Robbins et al., 1973)**. **Peltola in 1984** found that ninety four percent of cases with bacteremic H. influenzae infections are children under 10 years of age **(Peltola et al., 1984)**. Ninety five percent of Hib disease happens in children below 5 years of age **(Makela et al., 1992)**. Children with epiglottitis due to Hib are on average older than those with other Hib infections; nearly all are over one year old and mostly between 2 and 7 years old **(Turk, 1984)**.

Seasonal variation in Hib disease suggested a viral coinfection or preceeding infection **(Makela et al., 1992)**.

Ross et al., in 1992 reported that more than 18% of 440 patients with measles developed laryngotracheo-bronchitis. The likelihood that it would complicate measles was inversely related to age; the younger the age the higher the incidence of croup.

In **1974, Floyd et al.,** found that low family income and low education level of parents were associated with increased risk of Hib disease. Again, this effect disappeared when other factors as breast feeding were controlled **(Cochi et al., 1986)**. The epidemiologic feature of Hib disease was not influenced by the nutritional status **(Mulla et al., 1984)**. The socioeconomic risk factors for Hib disease were divided by

Takala and Clements in 1992 into those affecting the child's susceptibility (short duration of breast feeding, parental smoking, previous hospitalization and history of otitis media) and those affecting his exposure to Hib bacteria (day care attendance **(Wenger et al., 1990 and Clements et al., 1992)**, crowded house holds **(Petersen et al., 1991)** and the presence of young siblings **(Istre et al., 1985)**. Paternal smoking is known to increase the risk of all respiratory infections **(Pedreira et al., 1985)**. The effect of maternal smoking is striking and perhaps best explained by the fact that the mother, more than the father, remains at home with children **(Istre et al., 1985)**. Children below 5 years of age who attend a Day Care Center/Nursery are 1.7-1.9 times more likely to develop Haemophilus influenzae infections than are children who do not attend **(Redmond and Pichichero, 1984; Istre et al., 1985)**. The only protective factor for invasive Hib disease described so far in deed breast feeding **(Lum et al., 1982; Cochi et al., 1985; Istre et al., 1985 and Petersen et al., 1991)**. The mechanism of protection was proved that breast feeding enhance immune responses to Hib **(Pabst and Spady, 1990 and Brandtzaeg and Kett, 1992)**.

Aetiology:

Viral croup is most commonly caused by parainfluenza viruses (75%). Adenoviruses, respiratory syncytial, influenza, and measles viruses are behind a quarter of viral croup cases **(Nelson, 1992)**.

In 40% of Australian **(Gilbert et al., 1990)** and Finish **(Takala and Clements, 1992)** children below 5 years of age

and with epiglottitis - the cardinal disease of croup - Haemophilus influenzae type b was the cause, while some american authors **(Dajan et al., 1979)** reported slightly lower percentages. **Valdepena et al., in 1995** in Pittsburgh, found Haemophilus influenzae type b behind 21 cases out of 28 children with epiglottitis. Hib infection is transmitted most commonly via droplets followed by oro- and naso-pharyngeal colonization **(Beachey, 1981)**. The nasopharyngeal carriage rate of Hib was not found particularly high in populations with high rates of Hib disease **(Ward et al., 1981)**. The carriage rate of Hib in European children declined substantially after widespread vaccination with conjugated Hib vaccine **(Mohle-Boetani et al., 1993)**. **Sung et al., 1995** reported a relatively low carriage rates of Hib among Chinese children and postulated a quantitative or qualitative deficiency of secretory immunoglobulin A in their nasopharyngeal secretion. Many cases of croup caused by Hib bacteria are known to follow respiratory viral infections.

In 1893 Pfeiffer claimed that Haemophilus influenzae organism caused influenza; yet the full range of pathogenic activities of this species became clear in the period 1930-1960 **(Turk, 1984)**. It is interesting to remember that just a minority H. influenzae strains have polysaccharides capsules. Only one of the six capsular types which is type b differs in the pathogenicity from the rest of the species at least as markedly as do streptococci group A from other B-hemolytic streptococci. In fact, the five non b capsulated strains (a and c-f) can be regarded as non-pathogens.

The natural habitat and reservoir for Hib bacteria are the upper respiratory mucosal surfaces, primarily the

nasopharynx. Hib bacteria represent part of the normal nasopharyngeal flora. **Farley and Stephens in 1992** considered nasopharyngeal colonization by Hib as (1) a source of transmission to other susceptible individuals, (2) a source of infection of adjacent anatomic sites and especially epiglottitis, and (3) a probable site of mucosal invasion proceeding systemic disease. They claimed that the nasopharyngeal mucus may contain components that specifically bind Hib producing a cytotoxicity characterized by breakdown of junctions of epithelial cells, sloughing of ciliated cells and ciliostasis. Hib attach selectively to non ciliated cells and reach the submucosa primarily by an intercellular route **(Farley and Stephens, 1992)**. Wilson et al. in 1992 **(Wilson et al., 1992)** attributed the invasion by Hib bacteria to respiratory epithelial damage and slowed mucocillary clearance following viral infection or cigarette smoking.

Immunoglobulins:

The level of immunoglobulins in children passes through a critical period when the passively acquired antibodies from the mother are exhausted **(Fothergill and Wright, 1933)**. This period characterized by low protection standard ends when the child's own antibody production starts. Children begin the production of immunoglobulins against Haemophilus influenzae type b on exposure **(Peltola et al., 1977)**. Maternal antibodies are responsible for the infrequency of haemophilus meningitis in the first two months of life **(Turk et al., 1984)**.

Differences in immunological responsiveness in patients with acute epiglottitis and meningitis have been elaborated in the literature. While **Sly et al. in 1988** could detect IgG and

IgM serum antibody to non-capsular H. influenzae antigens in cases of both infectious diseases at presentation, most investigators **(Whisnant et al., 1976 and Rosales et al., 1984)** reported absence of serum antibody to capsular polysaccharide of Hib bacteria in the acute phase and after 14 days of meningitis in contrast to its presence and rise in cases of epiglottitis. Yet, the absence of rise of convalescent serum antibody titres in patients with meningitis in comparison with those with epiglottitis has been a constant finding in literature. These serological immune differences between acute epiglottitis and meningitis suggest that the child's immunological ability to respond to challenge with H. influenzae may determine the nature and site of the infection that results. It may be related to the child's age, the degree of his previous exposure to Hib bacteria or an underlying abnormality of the specific mucosal or systemic immune response to this organism.

Van Alphen et al. in 1983 found that the differences in Hib strains depending on their outer membrane components - proteins and lipopolysaccharide (LPS) - were not linkable to the incidence of the disease. Therefore, he could not consider bacterial virulence as an important risk factor.

The depletion of other defence mechanisms such as the complement system and phagocytosis in cases of asplenia has been shown to increase susceptibility to Hib disease **(Ward and Smith, 1976)**.

Clinical Aspect:

The clinical definitions of the lower respiratory tract infections put in 1975 by Moffet **(Moffet, 1975)** can be very helpful in the differential diagnosis. It is summarized as follow:

1. Laryngitis is recognized by hoarseness and laryngotracheobronchitis (croup) is characterized by brassy cough and inspiratory crowing.
2. Epiglottitis is defined by visualization of a red and edematous epiglottis associated with the pooling of oropharyngeal secretions and hoarseness.
3. Tracheitis is characterized by brassy cough (without hoarseness) and coarse breath sounds (without rales, rhonchi or wheezing).
4. Bronchitis is defined by the association of cough with coarse rhonchi that clear with coughing (with or without wheezing) but without audible rales. Rhonchi are coarse, moist popping sounds, usually occurring on inspiration, whereas rales are fine popping sounds at the end of inspiration.
5. Bronchiolitis is characterized by tachypnea, poor air exchange, low diaphragms, clinical evidence of expiratory difficulty, and coarse inspiratory or expiratory breath sounds throughout the chest.
6. Pneumonia is diagnosed on the basis of fine end-inspiratory rales (frequently associated with fever and cough) with or without roentgenographic confirmation.

In 1992, clinical manifestations of croup was reviewed in the textbook of Nelson and was put in a characteristic sequence of symptoms and signs as follows. At first, there is only a mild brassy cough with intermittent stridor sometimes

preceeded by mild upper respiratory symptoms. As obstruction increases stridor become continues and associated with nasal flaring and suprasternal, infrasternal, and intercostal retractions. Agitation and crying aggravate the condition. With airway compromise, air hunger and restlessness develop and then superseded by severe hypoxemia and weakness, increasing pulse and eventual death from hypoventilation. Any manipulation of the pharynx including the use of a tongue depressor should be deferred and oxygen should be administered until the patient is transferred to hospital where optimal management of the airway and shock is possible.

Investigations:

The diagnosis of croup is probable on the clinical grounds, direct viewing of the epiglottis may be indicated. Yet, in a seriously ill child this should be until complete cardiorespiratory support is available and definitive treatment can be carried out since some patients may have reflex laryngospasm and acute complete obstruction, aspiration of secretions, and cardiorespiratory arrest following examination of the pharynx. The diagnosis requires depressing the tongue to see the epiglottis. Laryngoscopy may be performed when appropriate equipment and personnel are present to control the airway and eventually provide ventilatory support.

Lateral roentgenogram of the nasopharynx and the upper airway is needed in suspected cases.

The serum antibody titers against H. influenzae type b rise after epiglottitis.

Management:

Prevention of croup should depend on getting children away from the recognized predisposing factors such as viral infections and Haemophilus influenzae type b infections transmitted via droplets in crowded day - care centers, nurseries and houses **(Redmond and Pichichero, 1984)**. Avoidance of passive smoking is an important prophylactic policy **(Pedreira et al., 1985)**. Raising the socioeconomic standard **(Floyd et al., 1974)** is a national target. Last but most important is restriction of artificial feeding; breast feeding as mentioned above is the only protective factor for invasive Hib disease described so far **(Lum et al., 1982; Istre et al., 1985; Cochi et al., 1985; Petersen et al., 1991)**.

Peltola et al. in 1984 **(Peltola et al., 1984)** claimed protection afforded by Hib vaccine through detecting high antibody serum levels for at least four years after vaccination. This period was shorter in younger children and therefore they recommended the capsular polysaccharide (CPS) vaccine after the age of 16 to 20 months. They also recommended re-vaccination by CPS at the age of two years for children initially vaccinated before the age of 16 months. One dose of vaccine at each time without boosters is effective. It has been proven that the CPS-protein conjugate vaccines such as Hib diphtheria toxoid conjugate and Hib tetanus toxoid conjugate (Hib-TT) induce higher antibody levels than the purified CPS vaccine **(Schneerson et al., 1980; Claesson et al., 1989)**. The advantage of HIB conjugate vaccines has been recently reconfirmed in 1995 by Pittsburgh children's hospital

(Valdepena et al., 1995) and in 1997 by New York State Hospitals **(Liptak et al., 1997).**

Children with croup are presented either to Clinics or Emergency Rooms. Three therapeutic modalities are available for the treatment of croup: humidified air, racemic epinephrine and adrenal corticosteroids. Maintaining at least 50% relative humidity in the child's room is recommended. If there is evidence of hypoxemia, a mist tent with supplemental oxygen may be helpful. Racemic epinephrine is administered by inhalation (0.25 ml / kg 2.25% epinephrine) can quickly reverse airway obstruction in children with moderate forms of croup. The patient needs to be monitored for rebound airway obstruction for at least 2 hours after administration. In severe forms of croup, dexamethasone (0.6 mg/kg) is administered intramuscularly. Dexamethasone is effective at decreasing the obstructive symptoms of croup, but its onset of action is approximately 6 hours after administration. Therefore, racemic epinephrine is often helpful until the steroids begin to take effect. Dexamethasone is administered intravenously when indicated. Dexamethasone is effective in decreasing the length and the severity of respiratory symptoms associated with croup. When intubation is necessary steroids reduced the duration of intubation and the need for reintubation **(Cruz et al., 1995).** The difficulty in breathing can be severe enough to indicate an urgent transoral or transnasal endotracheal intubation. Tracheostomies may rarely be required to save the patient's life. Assessment of arterial blood gases (ABGs) with the aid of a transcutaneous pulsoxymeter or serological laboratory tests is fundamental in some emergency situations. The need of intubation for croup children has an incidence as low as

0.5% to 4.8% as shown in the Australian and Canadian series of **Levison et al., 1982** and as high as 11% as shown in the American more recent series of **Ross et al. in 1992**.

Serum Antibody Titres in Croup Children:

Whisnant et al. in 1976 indicated that the initial antibody response to Hib CPS was higher in patients with epiglottitis than in patients of the same age with meningitis. In **1992, Trollfors et al.,** found that this difference in antibody levels disappeared 6-12 months after the diseases onset.

The antibody response to Hib CPS after both natural infection and vaccination with purified CPS or CPS-protein conjugate vaccines in most healthy children above 18 months old was found a combined IgG, IgM and IgA response with a predominance of IgG **(Norden et al., 1976 and Harada et al., 1985)**. The levels of IgG antibody were recorded as 3 to 7 times higher than the sum of IgM and IgA antibodies in children 6-18 month old. A short-lasting IgM response may also be missed if serum samples are obtained too late **(Trollfors et al., 1992)**.

Serum antibody concentrations significantly rose by 3 weeks after presentation in children with epiglottitis **(Sly et al., 1988)**. The combined IgG, IgM and IgA responses were found long-lasting still detectable 6-12 months after the onset of symptoms **(Trollfors et al., 1992)**.

While some authors **(Norden et al., 1976 and Rosales et al., 1984)** could not detect any immunological response to infection with Hib and to CPS vaccines in children below 18 months old, others **(Claesson et al., 1987 and Trollfors et al., 1992)** proved a transient IgM response in children as young as 7 months. So, the age below which no antibody response can be detected ranges between 6 and 24 months according to literature. **Whisnant et al. in 1976** mentioned that children below 18 months old responded to Hib CPS less than older children and did not produce IgG antibody response.

Some children above 18 months old and even some adults did not as well show any antibody response during the bacteremic stage of Hib disease. The non responders above 18 months old were considered initially unhealthy **(Kayhty et al., 1981)**.

The protective level of serum antibodies against Hib CPS after natural infection is considered to be between 0.1 and 0.15 microgram/ml **(Kayhty et al., 1983 and Santosham et al., 1987)**. Immunization with type b capsular polysaccharide protects against Hib diseases only in children above 18-24 months old **(Smith et al., 1973 and Peltola et al., 1977)**. If the purified polysaccharide is conjugated to protein, protection is effective at a much younger age **(Anderson et al., 1985)**. Hib vaccine has significantly reduced hospital admissions for Hib diseases in New York State between 1982 and 1993 **(Liptak et al., 1997)**.

Most investigators **(Whisnant et al., 1976 and Rosales et al., 1984)** reported absence of serum antibody to capsular

polysaccharide of Haemophilus influenzae bacteria in acute phase and after 14 days of meningitis in contrast to its presence and rise in cases of epiglottitis. Only **Sly et al., 1988** could detect IgG and IgM serum antibody to non-capsular Haemophilus influenzae antigens in cases of acute epiglottitis and acute meningitis at presentation.

Mellander et al., 1984 found that the adult level of salivary IgA is approached at about 12 months age. **Haworth and Dilling, 1966** detected IgA in saliva of 10 full-term infants at the age of 3 weeks, but none in any child younger than 12 days. They also showed that serum and salivary IgA developed independently and that salivary IgA did not change with age between 2 years and 14 years, but an increase with age was seen in serum IgA levels. **Selner et al., 1968** detected salivary IgA at 1 week of age and the adult levels were reached at 4 weeks of age in 92% of normal infants. **Burgio et al., 1980** could not detect salivary IgA in newborn infants, but did so in all normal children examined at the age of 2 months, the concentration of salivary IgA increased progressively with age and reached adult levels in unstimulated saliva by the age of 6 to 8 years. These different results can be explained by variations in techniques, in sampling, storage of samples and large individual variations may also play a role **(Mellander et al., 1984)**. To minimize the intra- and interindividual variation one should collect unstimulated whole saliva. Nevertheless, variations in salivary flow could cause fluctuations in immunoglobulin concentrations. Variations between individuals could also result from differences in antigenic exposure and capacity to respond. Storage by freezing at -20 °C and -70 °C left the

antibody levels unchanged even after 12 months, in contrast to earlier observations **(Brandtzaeg et al., 1970)**.

Sly et al., 1988 reported that the acute salivary IgA samples from children with epiglottitis did not differ significantly from control healthy children although children with meningitis had higher median acute salivary IgA concentration.

MATERIAL AND METHODS

- Study Population
- Case Group
- Control Group
- Samples Collection
- Characters of Immunoglobulins Plates
- Storage of Plates
- Laboratory Methods

Material and Methods

Study Population:

A population analysis was conducted in order to evaluate the risk factors of croup among children residing the north east districts of Cairo and visiting Mataria Teaching Hospital there, between March 1994 and December 1996. The study was based matched case - control.

Fifty-three children constituted the material of the study; 34 were suffering from croup and the remaining were healthy forming the control group. The patient age varied from one and half year up to twelve years old. Sex discrimination was not considered as a condition.

Case Group:

Thirty-four children were enrolled. Every child in this group fulfilled the criterion of the case definition; namely a child was considered to have croup only when he or she suffered from the peculiar brassy cough (croupy) with or without signs of respiratory distress due to a varying degree of laryngeal obstruction. These children were either consulting the out-patient clinics and the emergency room or admitted to the ward and Intensive Care Unit of the Pediatrics Department.

Finding of cases was not easy, because epiglottitis - the most serious form of croup - is a seasonal disease in Egypt. The majority of cases present at the beginngs of winter and

spring seasons; few sporadic cases appear all over the year. Many cases were missed as they were treated from acute respiratory distress in the emergency room and ICU during night shifts. Oxygen inhalation improves these cases and their rapid discharge from hospital is a common event.

A questionnaire was conducted with the patients and their relatives. The following informations were recorded: patient name, age, sex, social conditions, complaints, present history, past history and family history of respiratory problems. General and local examinations were carried out in the routine way. Two milliliters of blood and one milliliter of unstimulated saliva were collected in sterile test tubes from each child using sterile syringes.

Control Group:

A random sample of nineteen children residing in the study area and visiting the same hospital for having elective surgical operations represented this group. These children were free from any upper or lower respiratory problems. History and physical examinations as well as blood and saliva samples collection were all carried out as in the case group.

Samples Collection:

Samples of blood and saliva were collected from the croup patient group and the control children group. Complete aseptic conditions were fulfilled using sterile syringes and sterile test tubes. The collected blood, about 2 cm^3, was centrifuged to obtain a clear serum. The serum was stored

deep frozen. The collected saliva was centrifuged to deposit the cells. The centrifuged saliva was stored deep frozen.

The National Research Center purchased ready made kits from Hoechst Company in Cairo. Five plates belonged to assessment of serum IgA, 5 plates for serum IgM, 5 plates for serum IgG, and 3 plates for salivary IgA. Each plate contains 12 wells.

Characters of Plates:

NOR-Partigen IgA plate is used for determination of the serum immunoglobulin A concentration. The assay range is 0.42-6.34 g/L Behring. The code number is OSLMO3. NOR-Partigen IgG-HC plate is used for determination of the serum immunoglobulin G concentration. The assay range is 2.5-37.7 g/L Behring. The code number is OSLN. NOR-Partigen IgM plate is used for determination of serum IgM concentration. The assay range is 0.32-4.83 g/L Behring. The code number is OSLP. The LC-Partigen IgA plate has an assay range of 0.8-13.3 mg/dL (Behring). It is used for determination of salivary immunoglobulin A concentration. Each plate contains monospecific antiserum in a ready - for use - agarose-gel layer. The antiserum is obtained by immunization of rabbits (K), sheep (S), goats (Z), horses (P) or pigs (SW). The letters in brackets are used to indicate the species of animals. The used preservatives are sodium azide (maximum 1 g/L) and sodium p-ethyl-mercury-mercapto-benzene-sulfonate (maximum 0.1 g/L). The pack contained one twelve-well plate and approved by Paul-Ehrlich-Institute, Federal Office for Sera and Vaccines in Germany.

Storage of Plates:

All the plates were put in the vicinity of the deep-freeze compartment of the refrigerator. They were stored in their original unopened state at +2° to +8°C and were protected from freezing.

Laboratory work (Methodology):

The laboratory studies were done in the Child Health Laboratory at the National Research Center.

(A) Method of determination of serum IgA, IgM and IgG concentration:

The main principle of the method is that the human serum provided from the croup patient group and the control children group reacts with the specific antiserum present in the NOR-Partigen plate producing single radial immunodiffusion precipitate. The diameter of the obtained precipitate differs according to the serum immunoglobulin concentration.

The stored serum was taken out of the fridge few hours before starting the laboratory study in order to allow serum thowing. The serum of the croup patient group was subjected to a dilution of (1:1 or 1:2) using isotonic saline solution. The dilution was done to avoid getting a precipitate diameter outside the assay range of kits. The control children serum was not subjected to any dilution.

The stored immunodiffusion plates were taken out of the fridge just before starting the work. The cover of the

aluminum container was pulled off the plates. The opened plate was allowed to stand for about five minutes at room temperature for evaporation of any condensed water vapour which may have penetrate into the wells. The volume of serum required per well was 5 μl using the Partigen Dispenser - 5 μl instrument. The control serum for NOR-Partigen supplied ready with the kits was introduced into well number one. The remaining wells were filled with the undiluted thowed serum of the control children group and the diluted thowed serum of the croup patient group. A dilution of 1:1 or 1:2 was done for the serum of the croup patient group using isotonic saline solution in order to avoid getting a precipitate diameter outside the assay range of kits. After introduction of the specimens into the twelve wells of each plate, the plate was allowed to stand tightly closed by its own cover at room temperature for at least continuous 18 hours before taking any reading results.

The reaction between NOR-Partigen and studied serum resulted in a precipitate rings. Measurements of the precipitate rings diameter were taken twice. The first assessment was done 18 hours after filling the wells of each plate. The obtained first reading helps in early diagnosis. The second assessment should be done after attainment of the diffusion end point. The second evaluation for NOR-Partigen IgA and NOR-Partigen IgG plates was done two days after filling the wells. For NOR-Partigen IgM plates, the second evaluation, was taken five days from filling the wells. The diameter of the precipitate ring was measured using a special scaled magnifying lenz in millimeters. The scaled lenz is called Peak Scale Lupe 7x (made in Japan). It is scaled from 0 up to 20 millimeters.

Reading in millimeters were used to sort out the comparable immunoglobulin concentration in g/L (Behring) from special tables supplied with the kits. The accuracy of the results were checked by comparing them with the results of the control serum supplied with the specific NOR-Partigen plate.

(B) Method of determination of salivary IgA levels:

The protein standard serum LC-V is supplied with the kit serves as reference preparations for quantitative immunological determination of salivary immunoglobulin A concentration. The protein standard serum LC-V is a lyophilized stabilized mixture of sera from healthy adults. Its immunoglobulin A concentration is 0.136 g/L (Behring). It contains sodium azide (maximum 1 g/L) as a preservative and aprotinin (maximum 80,000 KIU/L) as a stabilizer.

The protein standard serum LC-V was stored, in the original state, unopened, at about +2 °C to +8 °C until it was used before its expiry date.

The protein standard serum LC-V was supplied as powder. It was reconstructed with exactly 0.5 ml of distilled water. It was not shaked too vigorously, in order to avoid the formation of foam. Three samples with different concentrations were made using this standard serum. The first sample was the undiluted solution in which the IgA concentration is 0.136 g/L (Behring). The second was a 1:1 dilution made by using isotonic sodium chloride solution as a diluent, that made IgA concentration 0.068 g/L. The third was a 1:3 dilution made by using isotonic sodium chloride solution, that made IgA concentration 0.034 g/L.

The LC-Partigen IgA plate contains α-chain specific antiserum which reacts with the human salivary sample producing single radial immunodiffusion precipitate rings. The precipitate diameters vary according to the concentration of the immunoglobulin A in the samples.

The LC-Partigen IgA plate was removed from the fridge before doing the laboratory study. Its lid of aluminum container was opened. The plastic container was removed from the plate. The opened plate was allowed to stand for five minutes at room temperature, for evaporation of any condensed water vapour that might have entered the wells during the storage period. The first three wells were filled with the three different dilutions of the protein standard serum LC-V (undiluted - 1:1 - 1:3). The remaining wells were filled with the salivary samples provided from the croup patients group and the control children group. The volume needed to fill each well was 20 μl. After filling all the twelve wells, the plate was allowed to stand opened for about ten to twenty minutes to allow full samples absorption. The plate was closed with its plastic lid and it was left at room temperature. The precipitate ring diameters were measured twice. The first measure was taken two days after filling the wells. It serves for early diagnosis of the precipitate diameters. The second measurement was taken three days after filling the wells. In the second measurement the end point of the immunodiffusion reaction is reached. The measurements were done using a special scaled magnifying lenz in millimeters.

The immunoglobulin A concentration in the salivary samples of the croup patients group and the control children group were determined by using a graph paper. This graph

paper was drawn using a horizontal scale that represents the know immunoglobulin A concentration of the protein standard serum. The vertical scale represents the measured precipitate ring diameter of the protein standard serum in cubic millimeters. The resultant graph was a straight line and as anticipated it intersects the vertical scale at a value of 21 ± 4.5 mm^2.

Data were subjected to some statistical analytic methods in order to verify their significance. These tests included Anova and Student's t-test according to the specific suitability of the test for each relation among studied data.

RESULTS

- **Socioeconomic and Clinical Data:**
  - . In croup children
  - . In control children
  - . Relative Risks
- **Serum Immunoglobulins Concentrations in Each Group and Comparison**
- **Salivary Immunoglobulin A Level in Each Group and Comparison**

RESULTS

Fifty-three children constituted the subjects of the study; thirty-four were having croup while the remaining were healthy children forming the control group. All the children were residing the north-east districts of Cairo and Visiting Mataria Teaching Hospital, between March 1994 and December 1996. The children age ranged from six months up to twelve years old.

Results of Socioeconomic and Clinical Study

1. In croup patients:

Studying the age incidence of croup, showed two peaks one around the age of 18 months and the other around the age of 50 months (Table 1a and Fig. 1).

Statistical analysis of patients having croup revealed that 88.2% were males and 11.8% were females (Table 1b).

The incidence of croup cases was mostly presented during the fall season. Eighty-five percent of croup cases presented during the months of October, November and December (Table 1C).

Table (1a): Age distribution in croup patients

Age in years	Number	Percent
1½	7	38%
2	6	
3	3	32%
4	6	
5	5	
6	1	
10	3	
11	2	
12	1	

Table (1b): Sex distribution in croup patients

Sex	Number	Percent
Male	30	88.2%
Female	4	11.8%

Fig. (1): Age incidence in croup patients.

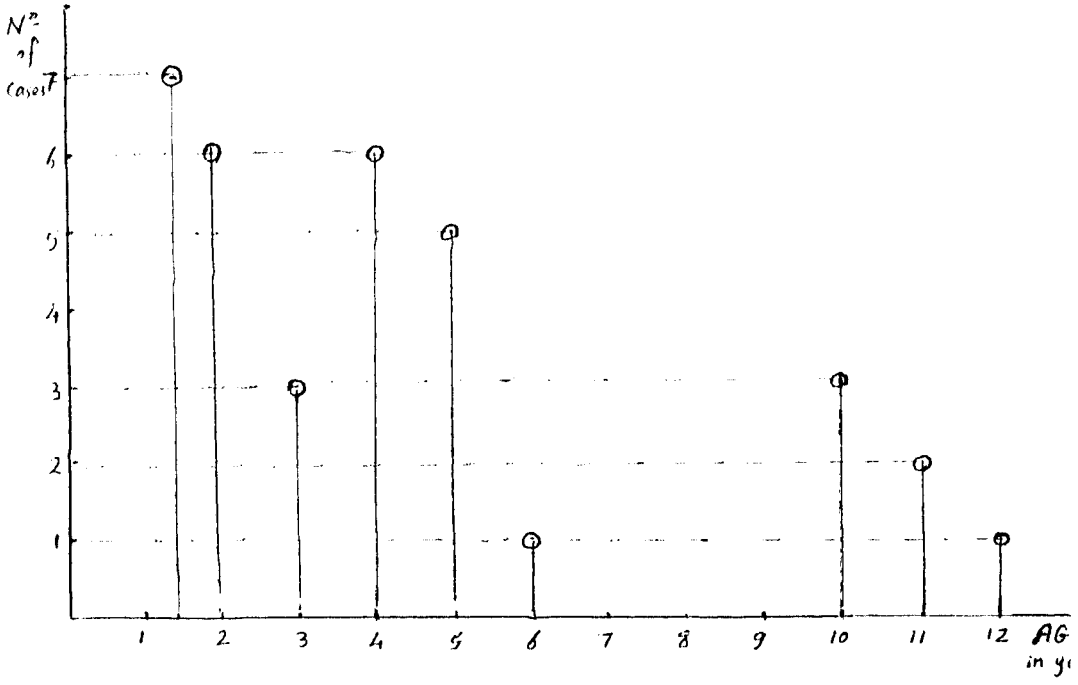

Table (1C): Seasonal incidence of croup.

Month	No. of cases	Percent
March	5	14.7%
October	14	41.2%
November	11	32.3%
December	4	11.8%

There were five predisposing factors that increased the host susceptibility to develop croup. Case survey showed that most of the patients (47%) had an attack of croup after sudden exposure to cold weather. One fifth of the patients developed croup attack after exposure to heavy smoke fumes. Twelve percent of the croup patients got an attack of croup following severe physical exercises. Only 2.9% of the cases contracted croup after drinking cold syrup, while 2.9% got the attack after being exposed to patients having respiratory tract infections. There was no history of any predisposing causes in 14.7% of the croup patients (Table 2).

Studying the frequency of the croup attacks in these patients revealed that the attack in 58.8% of cases was their first one, while 41.2% were having repeated croup attacks (Table 3).

Table (2): Predisposing factors in croup patients

Predisposing factor	Number	Percent
Exposure to cold weather	16	47%
Exposure to smoke fumes	8	23.5%
Severe physical exercises	4	11.8%
Drinking cold syrup	1	2.9%
Exposure to case with chest infection	1	2.9%
No history of predisposing causes	5	14.7%

Table (3): Frequency of croup attacks

Croup attack	Number	Percent
First attack	20	58.8%
Repeated attacks all the year	11	32.4%
Repeated attacks in winter	3	8.8%

History investigation revealed that 79.4% of croup children manifested their attack while other family member was having upper respiratory tract infection. In 44.1% of croup patients, history of previous hospitalization due to variable diseases was obtained within a week before contracting croup. (Table 4).

The socioeconomic data of the patients suffering from croup had been studied. It included the level of mother and father education, father's work, family income, family size and the degree of house crowdness. In 88% of croup patients the mother was either illiterate or didn't complete her primary education, while in 12% of cases the mother had attended the secondary school (Table 5). In 62% of croup cases the father did not complete his primary education and was working as manual worker while in 26% had completed his secondary education and in 12% he was a university graduate and was working as a government employee (Table 6).

On studying the family income, 35% had low income (less than 100 L.E./month), 44% had moderate income (100-400 L.E./month) and 21% had high income (more than 400 L.E./month) (Table 7). Each family was subjected to an analysis according to its size. Twenty-six percent of the families were having five or more children, 32% had three or four children and 41% had one or two children (Table 8). The house size and the degree of room crowdness had been studied. Fifty-six percent of the families declared that there

were three or more family members living in the same room while the remaining families had one or two members living in the same room (Table 9).

Fifty-three percent of croup children used to attend day-care facilities at the time of illness while 47% had never been to day-care units (Table 10).

Parental smoking contributed to the development of croup. Fifty-nine percent of the parents were smokers as compared to 41% who were non-smokers (Table 11).

Table (4): Past history in croup patients

Croup patients number	Croup patients with upper respiratory tract infection in family member	Percent
34	27	79.4%
Croup patients number	Croup patients with previous hospitalization of variable disease	Percent
34	15	44.1%

Table (5): Mother education of croup patients

Level of mother education	Number	Percent
Illiterate or did not complete primary education	30	88.2%
Attended secondary school	4	11.8%

Table (6): Father education of croup patients

Level of father education and his work	Number	Percent
Did not complete primary education - manual worker	21	61.8%
Completed secondary school - skilled labourer	9	26.5%
University graduate - government employee	4	11.8%

Table (7): Family income of croup patients

Family income	Number	Percent
Low income (< 100 L.E./month)	12	35.3%
Moderate income (100-400 L.E./month)	15	44.1%
High income (>400 L.E./month)	7	20.6%

Table (8): Family size of croup patients

Family size	Number	Percent
5 or more children	9	26.5%
3 or 4 children	11	32.4%
1 or 2 children	14	41.2%

Table (9): House crowdness of croup patients

House crowdness	Number	Percent
> 4 children/room	9	26.5%
3 or 4 members/room	10	29.4%
1 or 2 members/room	15	44.1%

Table (10): Day-care attendance of croup patients

Day-care attendance	Number	Percent
Attend day-care units	18	52.9%
Didn't attend day-care units	16	47.1%

Breast feeding study of croup patients showed that 91.2% of croup children had been breast fed for a period shorter than 18 months. breast feeding lasting beyond the age of 18 months was found in only 8.8% of cases (Table 12).

The presence of younger siblings in the families of croup patients was one of the risk factors that increased the tendency to develop repeated attacks. On analysis of the collected data, 68% of croup children were having younger siblings while 32% didn't have any younger siblings (Table 13).

On analysis of the clinical symptoms and signs of the croup patients, it showed that cough was the constant symptom in all croup patients. Sore throat was a common symptom with an incidence of above 80% among the croup patients. Almost all children with croup presented hoarseness of voice. Fever (body temperature above 38 °C) appeared in more than four fifths of patients. Forty-one percent of the patients were suffering from dyspnea. The occurrence of dysphagia was less than 50%. Cyanosis was a sign in only 2.9% of cases (Table 14).

Table (11): Parental smoking of croup patients

Parental smoking	Number	Percent
Smoker parents	20	58.8%
Non-smoker parents	14	41.2%

Table (12): Breast feeding duration in months for croup patients

Breast feeding in months	Number	Percent
<18 months	31	91.2%
≥ 18 months	3	8.8%

Table (13): The presence of younger siblings for croup patients

Patients having younger siblings	Number	Percent
have younger siblings	23	67.6%
don't have younger siblings	11	32.4%

Table (14): Clinical data of croup patients

Symptoms	Number	Percent
Cough	34	100%
Sore throat	28	82.4%
Hoarseness of voice	33	97.1%
Fever (> 38°C)	28	82.4%
Dysphagia	16	47.1%
Dyspnea	14	41.2%
Cyanosis	1	2.9%

2. In Control Children:

Control group was formed of nineteen healthy children. Their age ranged between 6 months and 12 years with the mean of 5 years. They were living in the North-East districts of Cairo and Visiting Mataria Teaching Hospital. Those children were free from any respiratory tract infection. Eighty percent of the control group were males and 20% were females (Table 15).

The socioeconomic data of the control group included the level of mother education, father education and the type of his work, the family income, family size and the degree of house crowdness. On studying the level of mothers education of control children group, 36.8% of the mothers were illiterate or had not had completed their primary education, 47.4% had attended secondary schools and 15.8% were university graduates (Table 16). The analysis of fathers education and their work showed that 10.5% had not had completed primary education and worked as manual workers, 52.6% had completed secondary school and worked as skilled labourers and 36.8% were university graduates and worked as government employees (Table 17).

On studying the family income, 15.8% of the families had low income (below 100 L.E. per month), 36.8% had moderate income (100-400 L.E. per month) and 47.4% had high income (above 400 L.E. per month) (Table 18). Each

family was subjected to an analysis according to its size. Only 10.5% of the control families were having five or more children, 36.8% were having three or four children while 52.6% were having one or two children (Table 19). Studying the house size and the degree of room crowdness showed that only 15.8% of the control families had more than four members living in one room, 31.6% of the control families had three or four members living in one room while 52.6% of the control families had one or two members living in the same room (Table 20).

Table (15): Sex distribution in control group

Sex	Number	Percent
Male	15	80%
Female	4	20%

Table (16): Mother education of control group

Mother education	Number	Percent
illiterate or did not complete primary school	7	36.8%
attended secondary school	9	47.4%
University graduates	3	15.8%

Table (17): Father education of control group

Father education	Number	Percent
Did not complete primary education - manual workers	2	10.5%
Completed secondary school - skilled labourers	10	52.6%
University graduates - government employee	7	36.8%

Table (18): Family income of control group

Family income	Number	Percent
Low income (<100 L.E./month)	3	15.8%
Moderate income (100-400 L.E./month)	7	36.8%
High income (>400 L.E./month)	9	47.4%

Table (19): Family size of control group

Family size	Number	Percent
5 or more children	2	10.5%
3 or 4 children	7	36.8%
1 or 2 children	10	52.6%

Table (20): House crowdness of control group

House crowdness	Number	Percent
>4 members/room	3	15.8%
3 or 4 members/room	6	31.6%
1 or 2 members/room	10	52.6%

Forty-two percent of the control children were attending day-care or nursery facilities as compared to 57.9% who had never been to the day-care units (Table 21).

Analysis of the parental smoking in the control children group revealed that 31.6% of the parents were smokers while 68.4% were non-smokers (Table 22).

Breast feeding studies of the control children group showed that 31.6% continued their breast feeding for more than 18 months age (Table 23).

The presence of younger siblings for control children group was studied. Forty-two percent of the control children group were having younger siblings as compared to 57.9% who didn't have any younger siblings (Table 24).

Table (21): Day-care or nursery attendance of control group

Day-care attendance	Number	Percent
Attend day-care	8	42.1%
Didn't attend day-care	11	57.9%

Table (22): Parental smoking of control group

Parental smoking	Number	Percent
Smoker parents	6	31.6%
Non-smoker parents	13	68.4%

Table (23): Breast feeding duration in months for control group

Breast feeding in months	Number	Percent
<18 month	13	68.4%
≥ 18 month	6	31.6%

Table (24): The presence of younger siblings for control group

Children having younger siblings	Number	Percent
have younger siblings	8	42.1%
don't have younger siblings	11	57.9%

3. Socioeconomic comparison between children in the croup and the control groups:

Risk factors:

Comparison between nine socioeconomic conditions in croup children and control children groups revealed that all the nine parameters contributed as risk factors in croup aetiopathogenesis. Three factors were strongly related to croup incidence. These were the level of mother education, the level of father education, and the duration of breast feeding.

Croup children whose mothers were illiterate, were at risk of attracting croup 12.87 times than those children whose mothers had completed their education. This relation was statistically significant (P-value = 0.0002). Children whose fathers were illiterate were at risk of getting croup 4.36 folds than those children whose fathers had completed their education. This factor was statistically significant (P-value = 0.001). Children who were breast fed for less than 18 months had a relative risk of getting croup 4.78 folds than those fed for longer duration. This factor was statistically significant (P-value = 0.001) (Table 25).

Children living in families with low to moderate income were at risk of getting croup 3.48 times than those children living in families with high income (Table 25). Croup children with smoker parents were at risk of getting croup 3.10 times than those with non-smoker parents. Croup

children having younger siblings were at risk of getting croup attacks 2.9 times than those without younger siblings. Children who were attending day-care units were at risk of contracting croup 1.54 folds than those who didn't attend such units. Children living in families having five or more kids were at risk of croup attacks 1.59 times than those families having less number of kids. Children living in families having more than four members per room were at risk of getting croup 1.41 folds than those children with less house crowdness (Table 26).

Table (25): Comparative study between croup patients and control in relation to risk factor.

Mother education	Control	Croup	Odds ratio	P-value
Mother completed school education	12 (75%)	4 (25%)	1.00	
Illiterate mother	7 (18.9%)	30 (81.1%)	12.87	0.0002
Father education and work				
University graduate government employee	7 (63.6%)	4 (36.4%)	1.00	
Illiterate or completed secondary school Manual or skilled worker	12 (28.6%)	30 (71.4%)	4.36	0.001
Family income				
High	9 (56.25 %)	7 (43.75 %)	1.00	
Low or moderate	10 (27%)	27 (73%)	3.48	0.09
Breast feeding				
Children breast fed for ≥ 18 month	6 (66.7%)	3 (33.3%)	1.00	
Children breast fed for < 18 month	13 (29.5%)	31 (70.5%)	4.78	0.001

Table (26): Comparative study between croup patients and control in relation to risk factors.

Parental smoking	Control	Croup	Odds ratio	P-value
Children without parental smoking	13 (48.1%)	14 (51.9%)	1.00	
Children with parental smoking	6 (23%)	20 (77%)	3.10	0.1
Younger siblings				
Children without younger siblings	11 (50%)	11 (50%)	1.00	
Children with younger siblings	8 (25.8%)	23 (74.2%)	2.87	0.1
Day-care				
Children don't attend day-care	11 (40.7%)	16 (59.3%)	1.00	
Children attend day-care	8 (30.8%)	18 (69.2%)	1.54	0.6
Family-size				
5 or more children	10 (41.7%)	14 (58.3%)	1.00	
4 or less children	9 (31%)	20 (69%)	1.59	0.6
House crowdenss				
>4 members/room	10 (40%)	15 (60%)	1.00	
≤3 members/room	9 (32.1%)	19 (67.9%)	1.41	0.5

Serum Immunoglobulin Concentration

The serum immunoglobulins concentrations of the croup children group, as compared to the control children group, showed considerable rise in all types of immuoglobulins.

Serum immunoglobulin A concentration in croup patients ranged between 0.702 g/L and 3.930 g/L with the mean of 1.529 ± 0.778 g/L. In control children, it ranged between 0.420 g/L and 3.190 g/L. The median was 1.187 g/L in the croup children as compared to 0.854 g/L in the control children (Table 27).

Serum immunoglobulin G concentration in croup children ranged between 5 g/L and 25 g/L with the mean of 14.294 ± 5.314 g/L. In control children, it ranged between 5.080 g/L and 16.940 g/L with the mean of 11.006 ± 3.645 g/L. The median was 13.430 g/L in the first croup and 12.500 g/L in the second group (Table 28).

Table (27): Serum immunoglobulin A for case and control

	Mean	Std. Dev.	Minimum	Median	Maximum
Case	1.529	±0.778	0.702	1.187	3.930
Control	1.065	±0.681	0.420	0.854	3.190

P-value = 0.032

Table (28): Serum immunoglobulin G for case and control

	Mean	Std. Dev.	Minimum	Median	Maximum
Case	14.294	±5.314	5.000	13.430	25.000
Control	11.006	±3.645	5.080	12.500	16.940

P-value = 0.019

Table (29): Serum immunoglobulin M for case and control.

	Mean	Std. Dev.	Minimum	Median	Maximum
Case	1.483	±0.660	0.640	1.360	2.9
Control	1.190	±0.327	0.833	1.090	1.92

P-value = 0.072.

Serum immunoglobulin M concentration in croup children ranged between 0.64 g/L and 2.9 g/L with the mean of 1.483±0.66 g/L. In control children, it ranged between 0.833 g/L and 1.920 g/L with the mean of 1.190±0.327 g/L. The median was 1.360 g/L for croup children and 1.09 g/L for control group (Table 29).

Children of croup patients group and those of control group were grouped into three main subgroups according to the age for better analysis of the results of serum immunoglobulins concentration. The first group included children below the age of twenty-five months. The second group included children whose age between twenty-five months and sixty months. The third group included children whose age was more than sixty months. The serum immunoglobulins A, G and M rose in croup patient group as compared to the control group. This rise was age dependent with wide individual variations. The rise of immunoglobulins increased with age (Tables 30-35).

The serum immunoglobulin A concentration in croup children aged below 2 years ranged between 0.702 g/L and 1.554 g/L with the mean of 1.026 ± 0.232 g/L. In croup children aged between 2 and 5 years it ranged between 0.84 g/L and 2.7 g/L with the mean of 1.491 ± 0.601 g/L. In croup children above 5 years old, it ranged between 0.854 g/L and 3.93 g/L with the mean of 2.294 ± 0.991 g/L (Table 30).

The serum immunoglobulin G concentration in croup children aged below 2 years ranged between 9.24 g/L and 16.04 g/L with the mean of 12.254 ± 1.930 g/L. In children aged between 2 and 5 years

it ranged between 5 g/L and 24.92 g/L with the mean of 13.683 ± 6.118 g/L. In children above 5 years old, it ranged between 10.16 g/L and 25 g/L with the mean of 18.245 ± 5.267 g/L (Table 31).

The serum immunoglobulin M concentration in croup children aged below 2 years ranged between 0.647 g/L and 2.320 g/L with the mean of 1.278 ± 0.485 g/L. In children aged between 2 and 5 years it ranged between 0.64 g/L and 2.9 g/L with the mean of 1.527 ± 0.695 g/L. In children above 5 years old, it ranged between 0.64 g/L and 2.6 g/L with the mean of 1.684 ± 0.795 g/L (Table 32).

The serum IgA, IgG and IgM concentrations in the control children as distributed in 3 comparable age subgroups are figured in Tables (33-35).

Table (30): Serum immunoglobulin A for age subgroups in croup patients.

Age subgroups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	1.026	±0.232	0.702	0.976	1.554
2 (>2-5 y)	1.491	±0.601	0.840	1.260	2.700
3 (>5-12 y)	2.294	±0.991	0.854	2.440	3.930

P-value = 0.0009

Table (31): Serum immunoglobulin G for age subgroups in croup patients.

Age subgroups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	12.254	±1.930	9.240	11.91	16.04
2 (>2-5 y)	13.683	±6.118	5.000	14.00	24.92
3 (>5-12 y)	18.245	±5.267	10.16	20.03	25.00

P-value = 0.037

Table (32): Serum immunoglobulin M for age subgroups in croup patients.

Age subgroups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	1.278	±0.485	0.647	1.300	2.32
2 (>2-5 y)	1.527	±0.695	0.640	1.542	2.90
3 (>5-12 y)	1.684	±0.795	0.640	1.732	2.60

P-value = 0.59

Table (33): Serum immunoglobulin A for age subgroups in control children.

Age groups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	0.512	±0.107	0.420	0.488	0.629
2 (>2-5 y)	0.902	±0.332	0.420	0.854	1.530
3 (>5-12 y)	1.755	±0.952	0.777	1.350	3.190

P-value = 0.01

Table (34): Serum immunoglobulin G for age subgroups in control children.

Age subgroups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	6.873	±1.733	5.080	7.000	5.080
2 (>2-5 y)	10.595	±3.241	5.540	12.500	12.500
3 (>5-12 y)	14.388	±2.115	11.320	14.340	11.320

P-value = 0.007

Table (35): Serum immunoglobulin M for age subgroups in control children.

Age subgroups	Mean	Std. Dev.	Minimum	Median	Maximum
1 (0-2 y)	1.237	±0.183	1.030	1.300	1.380
2 (>2-5 y)	1.115	±0.359	0.833	0.962	1.920
3 (>5-12 y)	1.329	±0.318	0.833	1.380	1.600

P-value = 0.5

The effect of the frequency of croup attacks on serum level of immunoglobulin A, G, and M was studied. The croup patients were grouped into two main groups. The first group included croup patients who were having their first croup attack during study conduction. The second group included croup patients who were accustomed to have repeated attacks of croup allover the year. The number of croup children with the first attack was twenty and those children who had repeated attacks were fourteen. The mean value of serum immunoglobulin A for the first group was 1.253 ± 0.549 g/L and for the second group was 1.924 ± 0.899 g/L. This relation was statistically significant with P-value of 0.01 (Table 36). The mean value of serum immunoglobulin G for the first group was 12.238 ± 5.022 g/L and for the second group was 17.230 ± 4.361 g/L. This relation was statistically significant with P-value of 0.005 (Table 37). The mean value of serum immunoglobulin M for the first group was 1.231 ± 0.506 g/L and for the second group was 1.843 ± 0.633 g/L. This relation was statistically significant with the P-value of 0.005 (Table 38).

The effect of fever in croup patients on serum level of immunoglobulin A, G and M was studied. Twenty eight children were feverish (>38 °C) and the remaining six had normal body temperature. The mean value of serum immunoglobulin A for feverish croup patients was 1.611 ± 0.824 g/L while the mean for non-feverish croup patients was 1.147 ± 1.554 g/L. The relation was statistically insignificant

(P-value = 0.237) (Table 39). The mean value of serum immunoglobulin G for feverish croup patients was 14.843 ± 5.401 g/L and for non-feverish croup patients was 11.730 ± 4.388 g/L. The relation was statistically insignificant (P-value = 0.194) (Table 40). The mean value of serum immunoglobulin M for feverish croup patients was 1.578 ± 0.677 g/L was compared to that of non-feverish croup patient which was 1.042 ± 0.336 g/L. This was statistically insignificant (P-value = 0.06) (Table 41).

Table (36): Effect of frequency of croup attacks on serum IgA in croup patients.

Attack frequency	No. of pts.	Mean	Std. Dev.	Minimum	Median	Maximum
First attack	20	1.253	±0.549	0.702	1.046	2.700
Repeated attacks	14	1.924	±0.899	0.840	1.903	3.930

P-value = 0.01

Table (37): Effect of frequency of croup attacks on serum IgG in croup patients.

Attack frequency	No. of pts.	Mean	Std. Ved.	Minimum	Median	Maximum
First attack	20	12.238	±5.022	5.000	11.975	25.00
Repeated attacks	14	17.230	±4.361	11.080	17.640	24.920

P-value = 0.005

Table (38): Effect of frequency of croup attacks on serum IgM in croup patients.

Attack frequency	No. of pts.	Mean	Std. Dev.	Minimum	Median	Maximum
First attack	20	1.231	±0.566	0.640	1.184	2.460
Repeated attacks	14	1.843	±0.633	0.650	1.732	2.900

P-value = 0.005

Table (39): Effect of fever on serum IgA in croup patients

Presence of fever	No. of pts.	Mean	Std. Dev.	Minimum	Median	Maximum
Patients with fever	28	1.611	±0.824	0.702	1.258	3.930
Patients without fever	6	1.147	±0.332	0.840	1.046	1.554

P-value = 0.237

Table (40): Effect of fever on serum IgG in croup patients

Presence of fever	No. of pts.	Mean	Std. Dev.	Minimum	Median	Maximum
Patients with fever	28	14.843	±5.401	5.000	14.000	25.00
Patients without fever	6	11.730	±4.388	5.820	11.080	19.24

P-value = 0.194

Table (41): Effect of fever on serum IgM in croup patients

Presence of fever	No. of pts.	Mean	Std. Dev.	Minimum	Median	Maximum
Patients with fever	28	1.578	±0.677	0.640	1.542	2.900
Patients without fever	6	1.042	±0.336	0.640	1.072	1.420

P-value = 0.06

Salivary Immunoglobulin A

Salivary samples collected from croup children and control children was studied. The immunog-lobulin A level in saliva of croup children during the attack was not significantly different from the level in control children. The mean value of salivary immunoglobulin A of croup patients was 0.0846 g/L while the mean value of salivary immunoglobulin A of control children was 0.0828 g/L (Table 42).

Table (42): Salivary IgA in croup and control groups

	Sample number	Mean	Std. Dev.	Minimum	Maximum
Croup patients	18	0.084660	±0.07	0.022	0.176
Control children	8	0.082875	±0.08	0.004	0.176

DISCUSSION

- **Concerning:**
  - **Demographic Profile**
  - **Socioeconomic Parameters**
- **Serum Immunoglobulins**
- **Salivary Immunoglobulin A**

Discussion

Fifty-three children constituted the subjects of the study; 34 were having croup while 19 were healthy children forming the control group. They were visiting Mataria Teaching Hospital, between March 1994 and December 1996.

Studying the immunological pattern in croup patients is considered an important element for understanding the pathology and the diagnosis of croup disease. Concentrations assessment of different serum and salivary immunoglobulins can as well be useful for precise evaluation and study of intensity of croup disease during its course.

Age:

The results of this work revealed two peaks one around 1½ year and another around 4½ years. This results go with most of result written in literatures. The peak incidence of age in patients with epiglottitis occurs at 2½ to 3 years **(Robbins et al., 1973)**. In fact, the young age represents the most important risk factor for Hib disease **(Peltola et al., 1977)**. Young age is associated with the highest incidence, but passive protection of some infants by transplacentally acquired maternal antibody is thought to delay the peak attack rates until the age of 6 or 7 months **(Cochi et al., 1985)**. **Peltola et al. in 1984** found that ninety-four percent were children under 10 years of age. **Makela et al. in 1992** found that ninety-five percent of Hib disease happened in children below

5 years of age. Children with epiglottitis due to Hib are on average older than those with other Hib infections, nearly all are over one years old and mostly between 2 and 7 years **(Turk, 1984)**. The age-specific incidence curve was found shifted to the left in populations with especially high incidence of Hib diseases as in Alaskan Eskimos and in the White Moutain Apaches **(Ward et al., 1981 and Losonsky et al., 1984)**, or it was shifted to the right in populations with lower attack rates as in Swedish region **(Peltola et al., 1984 and Claesson et al., 1984)**.

Gender:

Statistical analysis of patients having croup revealed that 88% were males and 12% were females. This manifest male predominance is parallel to results of **Gilbert et al. in 1990** and **Takala and Clements in 1992**. The distribution of our cases by gender was not found statistically different from the study done by **Cochi et al. in 1986**.

Seasonal Variation:

The study revealed seasonal variation in the incidence of croup. Eighty-five percent of croup cases presented in the fall season. **Nelson, (1992)** and **Knott et al. (1994)** reported that the incidence of croup occurs most commonly during the cold and fall seasons.

Predisposing factors to croup disease:

The current study showed that sudden exposure to cold weather and to smoke fumes were the most frequent predisposing factors in the studied population. In two thirds of cases these factors were claimed as predisposing conditions. **Wilson et al. in 1992** reported that the invasion by Hib bacteria was attributed to respiratory epithelial damage and slowed mucociliary clearance that usually follows viral infections and exposure to cigarette smoking.

Frequency of croup attacks:

More than half of croup children in this study were manifesting their first attack during work conduction. Patients with repeated attacks did not claim seasonal incidence in 25% of cases, although those with the first attack were mostly seen during winter months. **Makela et al. in 1992** found seasonal variations in Hib disease and attributed that to viral co-infection or proceeding infection.

Past history in croup patients:

Forty-four percent of the studied croup cases reported previous hospitalization due to variable diseases and within a week before contracting croup. **Tarr and Peter in 1978** found that high hospitalization rate did not increase risk of Hib disease . **Takala et al. in 1989** couldn't deny the importance of this factor.

Three quarters of cases gave history of upper respiratory tract infection of a family member during their croup attack. **Stahlberg in 1980** and **Tainio in 1988**, found that a history of otitis media was more strongly associated with increased risk of Hib disease especially among children less than one year of age. **Istre et al. in 1985** didn't find any association between history of upper respiratory tract infection or otitis media and invasive Hib disease.

Socioeconomic conditions:

The socioeconomic conditions are known to influence the incidence of croup disease and its aetiopathological aspects. Literature points out nine socioeconomic risk factors related to croup disease. These nine risk factors were investigated in the current study. Results of this work came parallel to those published by many authors. Three factors namely the level of mother education, the level of father education and breast feeding for more than 18 months of age were found to be the only statistically significant risk factors in the current study.

The current study showed that low level of mother and father education were statistically significant risk factors that incresaed the risk to contract croup (P-value for the level of mother education = 0.0002 and for father education = 0.001). **Floyd et al. (1974)** reported that low level of parental education increased the risk for invasive Hib disease in urban and rural Tennessee. **Cochi et al. (1986)** and **Takala et al.**

(1989) didn't find association between the parental education and the socioeconomic status with the risk of Hib disease in the studies conducted in Finland in Victoria, Australia. However, the soecioeconomic status in these population is relatively homogeneous, so it was not surprising that statistically significant differences could not be found.

Children who stopped breast feeding before the age of 18 months had higher risk to develop croup as compared to those who continued breast feeding for more than 18 months of age, the same age of the incidence peak of croup. Breast feeding for more than 18 months of age was found protective against the incidence of croup disease in the current study (P-value = 0.001).

Pabst and Spady (1990) and **Brandtzaeg and Kett (1992)** proved that breast feeding enhance immune responses against Hib disease. The only protective factor for invasive Hib disease described so far is indeed breast feeding **(Lum et al., 1982; Istre et al., 1985; Cochi et al., 1986** and **Petersen et al., 1991)**. **Takala et al. in 1989** (Finland) reported that the protective effect of breast feeding lasted for more than 6 months, while **Istre et al. in 1985** and **Cochi et al. in 1986** (U.S.A.) stated that the protective effect of breast feeding was limited to infant less than 6 months of age. In Finland prolonged breast-feeding was common, up to 80% of mothers breast-fed for at least 6 months and 60% for 9 months, whereas in the United States only 27% of mothers breast-fed

for 6 months. In fact, the longer duration of breast-feeding may explain why invasive Hib disease occurs in Finland at a somewhat older age than in the United States. **Cochi et al. in 1986** found that breast-feeding led to a 59% reduction of the number of Hib disease cases in this age group (2 to 5 months age). Breast feeding for all children below 6 months of age could potentially reduce the risk for Hib disease by 92% in them. It remains unclear whether some protection against Hib disease may be conferred by breast feeding children 6 to 11 months of age, an age group in whom the peak incidence of Hib disease occurs.

The remaining six socioeconomic risk factors had a relatively weaker relations to croup disease. These are family income, day-care attendance, presence of younger siblings, parental smoking, family size and the degree of house crowdenss. Their odds ratio was 3.48, 1.54, 2.87, 3.10, 1.59 and 1.41 respectively. These ratios were calculated without controlling for confounding. **Redmond and Pichichero in 1984**, **Istre et al. in 1985** repeated that children below 5 years of age who attend day-care centers were 1.7-1.9 times more likely to develop Hib infections than those who did not attend these centers. **Takala et al. in 1989** stated that recent attendance of day-care outside the house was a special risk factor for invasive Hib disease among children less than 2 years of age. Hib disease is contagious. Published studies of secondary spread of Hib disease in contact of index case have documented a significant increase in the risk of illness in both

household crowdness and day-care classroom contacts **(Granoff and Basden, 1980; Redmond and Pichichero, 1984 and Fleming et al., 1985)**. **Cochi et al. in 1986**, calculated that 50% of invasive Hib was attributed to exposure to day-care. Day-care had the highest attributable risk for children <24 months of age. This increased relative risk was high in this age group and then exhibited a linear decline with increasing age, relative risk was not significantly elevated in children 3 years or older. The house hold crowdness was significantly associated with risk for Hib disease, it had an attributable risk of 18%.

The current study showed an odds ratio of 3.1 concerning parental smoking. **Pedreira et al. in 1985** demonstrated that parental smoking is known to increase the risk of all respiratory infections. **Wilsonet al. in 1992**, reported that excessive exposure to cigarette smoke cause damage to the respiratory epithelial mucosa and slowed mucociliary clearance. This reduces the host defenses and enhances the attachment and invasion of Hib and lead to an increased risk of croup. **Cochi et al. in 1986** and **Takala et al. in 1989** demonstrated no association between parental smoking with the risk for Hib disease.

The presence of younger siblings increased the risk of attracting croup in the current study with an odds ratio of 2.87. **Istre et al. in 1985** demonstrated that the existence of siblings less than 7 years of age was a risk factor for invasive

Hib disease and the risk was highest for children less than 1 year of age. **Cochi et al. in 1986** and **Takala et al. in 1989** found no association between the presence of school-age siblings and the risk of invasive Hib disease.

The low family income increased the risk of getting croup in the current study with an odds ratio of 3.48 (P-value = 0.09). **Istre et al. in 1985** and **Cochi et al. in 1986** from the United States found that low family income was not associated with incidence of croup.

Serum immunoglobulins:

The serum antibody response was studied in 34 patients having croup, aged from 6 months up to 12 years old. Serum sample was obtained from each patient during the first week after the onset of croup symptoms. There was a statistically signifiant rise in serum immunoglobulin A and G in croup patients (P-value = 0.032 and 0.019 respectively). There was a rise in serum immunoglobulin M in croup patients that was statistically non-significant. Immunoglobulin M can be considered as the first line of defence in response to infections but it is known that the immunoglobulin M response is short lasting that it may be missed if serum samples are obtained late **(Trollfors et al., 1992).**

The antibody response was age dependent with wide individual variations. Croup children showed rise in serum imunoglobulins A, G and M in response to the development

of croup attack. This rise becomes more manifest in older children. This relation was proven highly significant for immunoglobulin A (P-value = 0.0009) and significant for immunoglobulin G (P-value = 0.037).

The serum immunoglobulins concentrations rose in patients with repeated croup attacks to higher levels than in patients with the first attack. This relationship was statistically significant for immunoglobulins A, G and M (P = 0.01 for immunoglobulin A, P = 0.005 for immunoglobulin G and P = 0.005 for immunoglobulin M).

The serum immunoglobulins levels in croup patients were found higher in those with fever compared with patients without fever. This relationship was tested statistically and proven non-significant as regards to the immunoglobulin A, G and M.

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Norden et al. in 1976, Harada et al. in 1985 and **Trollfors et al. in 1992** recorded that the antibody responses to Hib CPS (capsular polysaccharide of Hib bacteria) after both natural infection and vaccination with purified CPS or CPS-protein conjugate vaccines in most healthy children above 18 months old was found a combined immunoglobulin A, G and M response with a predominance of immunoglobulin G.

Norden et al. in 1976 and **Rosales et al. in 1984** could not detect any immunological response to Hib infection and to CPS vaccines in children below 18 months, while **Claesson et al. in 1987** and **Trollfors et al. in 1992** proved a transient immunoglobulin M response in children as young as 7 months.

The protective level of serum antibody against Hib CPS after natural infection has been determined as between 0.1 and 0.15 microgram/ml **(Kayhty et al., 1983 and Santosham et al., 1987)**. **Smith et al. in 1973** and **Peltola et al. in 1977** claimed that immunization with type b capsular polysaccharide protects against Hib disease only in children above 18 and 24 months old. **Anderson et al. in 1985** found that if the purified polysaccharide is conjugated to protein, protection is effective at a much younger age.

Salivary immunoglobulin A:

The current study proved that the immunoglobulin A level in saliva of croup patients during the attack was not different from the level of salivary immunoglobulin A in control children. The same findings were reported by **Sly et al. in 1988** who found that the acute salivary immunoglobulin A samples from patients with epiglottitis did not differ significantly from control healthy children.

Conclusion And Recommendations

The study demonstrated significant rise in serum immunoglobulins A and G with croup disease. There was a rise in immunoglobulin M as well, yet this rise was statistically non-significant as the immunoglobulin M is a short-lasting immunoglobulin.

The rise in serum immunoglobulins A, G and M was age dependent with wide individual variations. This rise became more manifest in older children. This relation was proven highly significant for immunoglobulin A and significant for immunoglobulin G.

The serum immunoglobulin A, G and M concentrations rose significantly in patients with repeated croup attacks.

The serum immunoglobulin A, G and M concentrations rose more in croup patients with fever than in those without fever. This was statistically insignificant for all types of immunoglobulins.

The salivary immunoglobulin A of croup patients during the acute attack was not different from the level of salivary immunoglobulin A in control children.

The rise in immunoglobulins level in croup patients proved in this study, should be considered as a protective

response. Recommendation for active immunization with type b capsular polysaccharide protects against Hib disease.

Additionally, the study demonstrated two socioeconomic conditions namely the level of mother education and the level of father education as statistically significant risk factors. Breast feeding for more than 18 months of age was found protective against the incidence of the disease with statistical significance. Low family income, the day-care attendance, the presence of younger siblings, the parental smoking and the house crowdness, without controlling for confounding, were found relatively weak risk factors.

Additionally again, the study supported the following four demographic points related to croup:

1. two peaks for age incidence around 18 and 50 months,
2. male predominance,
3. exposure to smoke fumes and to sudden change in weather as predisposing factors, and
4. seasonal (fall) incidence frequency.

SUMMARY

SUMMARY

The aim of this work was put to study the changes in serum and salivary immunoglobulins expected in early days of croup attack in children.

Thirty-four children presented with croup attack constituted the material of this study. The level of their immunoglobulins was compared with the level in nineteen healthy children residing the same districts in Cairo. The relations between the rises of immunoglobulins and different demographic and socioeconomic conditions were assessed. Statistical tests were performed to identify significance.

Results in croup children showed significant rise of serum immunoglobulins A, G and non-significant rise of serum immunoglobulin M because it is a short lasting immunoglobulin. The rise in serum immunoglobulins A, G and M was age dependent with wide individual variations and it became more manifest in older children. Repeated attacks significantly induced higher levels of immunoglobulins A, G and M. Fever rose the concentration of all types of immunoglobulins, insignificant relationship. The salivary immunoglobulin A was not found to be raised with croup.

Recommendations are driven from studying the demographic and the socioeconomic conditions. In order to reduce croup incidence, authorities should work for:

1. active vaccination with capsular polysaccharide conjugated to protein against Hib disease.
2. keeping on breast feeding for more than 18 months,
3. raising the level of mother and father education,
4. improving the level of family income, and
5. trying to keep children away from exposure to smoke fumes and sudden changes of weather.

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Sheet for croup children study

Sheet for Group Children Study

No.: Case No.
DATE
Name (Arabic) Address Telephone No. Sex Age in years Occupation
PRESENT HISTORY
Complaint Onset Course Duration (days) Cough Expectoration Expector colour Haemoptysis Dyspnea Chest pain Cyanosis Fever >38.5 Rhinitis Conjunctivitis Sore throat Dysphagia Drooling Hoarseness of voice Stridor G.I.T. symptoms Urinary symptoms Neurol. symptoms

PAST HISTORY

Repeated similar attacks
Allergy
Rash (measles)
Drug intake
F.B. inhalat.
Past hospital.
Past operation

FAM.HIS.(URTI)
(Upper respiratory tract infection)

SOCIAL HISTORY
Mother education level
Father education level
Family income
Family size
House crowdness
Daycare availability
Parental smoking
Younger siblings
Breast feeding (months)
Exposure to cold weather
Exposure to smoke fumes
Severe physical exercises
Drinking cold syrup
Exposure to case with chest infection
No history of predisposing causes

Investigations:
Throat swab and culture
chest X-ray
Serum immunoglobulins
Salivary immunoglobulin

GENERAL EXAMIN.
H.R. (beat/min.)
P.R. (cycle/min.)
Temp. (°C)
B.P. (mm/Hg)
Consciousness level
Decubitus
Cyanosis
Puffy eyelids
CHEST (L. EXAMIN.)
Shape
Retractions
Pulsations
Pigmentations
Dilated Vs.
Scars
Ulcers
Tenderness
Percussion
Auscultation

ARABIC SUMMARY

الملخص العربى

تهدف الدراسة إلى إثبات العلاقة بين التغيرات فى نسب تركيز الأجسام المضادة بالدم واللعاب من جانب ومرض الخناق فى الأطفال من جانب آخر . كما تهدف إلى تحديد علاقة هذه النسب مع عمر المريض ومع حالة أسرته الإجتماعيه والأقتصاديه.

كون أربعة وثلاثون طفلاً مصاب بمرض الخناق مادة هذه الدراسة. وقد قورنت كميات الأجسام المضادة بهم مع كمياتها فى تسعة عشر طفل سليم يسكنون نفس الأحياء بالقاهرة. وقد تم إختبار العلاقة بين زيادة الأجسام المضادة لهؤلاء المرضى وبين أعمارهم وجنسهم ومستوياتهم الإجتماعيه والإقتصادية. وقد تم تطبيق الأختبارات الأحصائية المناسبة لمعرفة درجة أهميه هذه العلاقات.

وقد أظهرت النتائج إرتفاع ذو أهميه احصائية فى الأجسام المضادة نوعية (أ) و (جـ). وإرتفاع غير احصائى فى الاجسام المضادة نوعية (م). وبدت الزيادة فى (أ) و(ب) و (جـ) أوضح فى الأطفال الأكبر عمراً. وقد ظهر أن تكرار الإصابة بمرض الخناق يؤدى إلى تكوين أجسام مضادة بكميات أكبر من الإصابة لأول مرة. كما وضح إرتفاع كميات الاجسام المضادة بصورة ملحوظة عندما تكون الإصابة مصحوبه بإرتفاع فى درجة الحرارة. وقد تبين أن الأجسام المضادة باللعاب لا تتأثر بالإصابه بمرض الخناق.

ودعت التوصيات للتقليل من الإصابة بالمرض بدعوة المسؤلين إلى العمل على:

١- تطعيم الأطفال عند سن ١٨ شهر بإستعمال مصل الأنفلونزا عديد السكرى الممزوج بالبروتين.

٢- رفع مستوى تعليم الأبوين.

٣- مد فترة الرضاعه الطبيعيه إلى أكثر من ١٨ شهر.

٤- تجنب تعريض الأطفال لدخان السجائر والتغيرات المفاجئة فى الجو.

مستخلص الرسالة

عنوان الرسالة
"دراسة الأجسام المضادة المناعية فى الأطفال المصابين بمرض الخناق"

أسم الباحث : الطبيبة / منال عبد المنعم مصر
مكان البحث : المركز القومى للبحوث ومستشفى المطرية التعليمى

كان الهدف من الرسالة هو دراسة العلاقة بين الأجسام المضادة المناعية و مرض الخناق فى الأطفال. ودراسة العلاقة بين الأجسام المضادة وعمر المريض وحالة أسرته الأجتماعية والأقتصادية.

وقد أشتملت الدراسة البحثية على مجموعيتن من الأطفال الذين تراوحت أعمارهم بين سنة ونصف وأثنى عشر سنة. مجموعة الأطفال المصابين بمرض الخناق وعددهم اربعة وثلاثون طفلاً، وقد تم أختيارهم من بين حالات دخول مستشفى المطرية التعليمى بقسم الأطفال. والمجموعة الأخرى تسعة عشر طفل من الأصحاء غير المصابين بأى من التهابات الجهاز التنفسى كمجموعة ضابطة.

وقد تم دراسة جميع الحالات من حيث تاريخ المرض والمستوى الاجتماعى والاقتصادى والفحص الأكلينيكى الدقيق المساعد على تحديد

الأصابة بمرض الخناق. وكذلك تم أجراء فحوصات معملية لتحديد نسبة الأجسام المضادة المناعية نوعية (أ) ، (ج) ، (م) فى الدم ونوعية (أ) فى اللعاب.

وقد استخلص من هذه الدراسة البحثية وجود علاقة ذو أهمية احصائية بين الأجسام المضادة بالدم والاصابة بمرض الخناق. وقد أظهرت النتائج زيادة نسبة الأجسام المضادة المناعية كلما زاد عمر المريض. وأن انخفاض مستوى التعليم للأبوين، وقصر مدة الرضاعة الطبيعية عن ثمانية عشر شهر، والتعرض المستمر لدخان السجائر والتغيرات المفاجئة فى الجو يزيد من معدل الاصابة بمرض الخناق.

الكلمات المفتاحية:

طب أطفال - جهاز تنفسى - حنجرة - مرض الخناق - أجسام مضادة مناعية.

جامعة عين شمس

الكلية:

شكر

أشكر السادة الأساتذة الذين قاموا بالأشراف وهم:

١- أ.د/ إسعاد يوسف خلاف - مستشفى المطرية التعليمى.

٢- أ.د/ إيمان عبد الوهاب العشماوى - المركز القومى للبحوث.

٣- د. / مجدى كرم الدين - جامعة عين شمس.

ثم الأشخاص الذين تعاونوا معى فى البحث وهم :

١- أ.د/ سلوى الحسينى - المركز القومى للبحوث.

٢- أ.د/ عزة جبر - المركز القومى للبحوث.

٣- أ.د/ سناء سعد البكرى - مستشفى المطرية التعليمى.

وكذلك الهيئات الأتية :

١- مستشفى المطرية التعليمى.

٢- المركز القومى للبحوث.

٣- معهد الدراسات العليا للطفولة - جامعة عين شمس.

جامعة عين شمس

الكلية:

صفحة العنوان:

أسم الطالب	:	منال عبد المنعم محسن.
الدرجة العليمة	:	دكتوراه.
القسم التابع له	:	الدراسات الطبيه.
أسم الكلية	:	معهد دراسات الطفولة.
الجامعة	:	جامعة عين شمس.
سنة التخرج	:	١٩٩٨.
سنة المنح	:	١٩٩٨.

شروط عامة:

يوضع شعار الجامعة على الغلاف الخارجى.

جامعة عين شمس

الكلية:

رسالة ماجستير / دكتوراة:

أسم الطالب : منال عبد المنعم محسن.

عنوان الرسالة : دراسة الأجسام المضادة فى الأطفال المصابين بمرض الخناق.

أسم الدرجة : (ماجستير / دكتوراه)

لجنة الإشراف:

١- الأسم / إسعاد يوسف خلاف ٢- الوظيفة / أستاذ ورئيس قسم الأطفال مستشفى المطرية التعليمى.

١- الأسم / إيمان عبد الوهاب العشماوى. ٢- الوظيفة / أستاذ مساعد طب الأطفال المركز القومى للبحوث.

١- الأسم / مجدى كرم الدين ٢- الوظيفة / مدرس بالقسم الطبى - معهد الدراسات العليا للطفولة.
جامعة عين شمس.

تاريخ البحث : ٢١/ ٢/ ١٩٩٤

الدراسات العليا

ختم الإجازة : / / ١٩ أجيزت الرسالة بتاريخ ٦ / ٥ /١٩٩٨

موافقة مجلس المعهد

٩٨/٦/١٧

جامعة عين شمس

معهد الدراسات الطبية العليا للطفولة

القسم الطبي

دراسة الأجسام المضادة المناعية في الأطفال المصابين بمرض الخناق

رسالة مقدمة من

الطبيبة / منال عبد المنعم محسن

توطئة للحصول على درجة دكتوراه الفلسفة في دراسات الطفولة

تحت اشراف

الأستاذة الدكتورة

اسعاد خلاف

رئيس قسم الأطفال

مستشفى المطرية التعليمي

الدكتورة

ايمان العشماوي

أستاذ مساعد طب الأطفال

المركز القومي للبحوث

الدكتور

مجدي كرم الدين

مدرس بالقسم الطبي لمعهد الدراسات العليا للطفولة

جامعة عين شمس

١٩٩٨