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2 **Editorial**
Ahmad Husari

Original Contribution / Clinical Investigation

3 **Case report: Heterozygous Familial Hypercholesterolemia (HeFH)**
Almoutaz Alkhier Ahmed

7 **Histological demonstration of Helicobacter Pylori (H Pylori) in patients with gastritis and Peptic Ulcer Disease (PUD) in Sulaimani**
Bahar Rasul Khdhir, Hiwa Banna, Michael Donald Hughson

17 **Nasal SIMV as an initial mode of respiratory support for premature infants with RDS. An observational study**
Ghassan S A. Salama, Aghadeer Alhadidi, Fadi F. Ayyash, Alia Khlefat , Elham S. Al Twall

24 **Efficacy of intravenous magnesium sulphate on postoperative pain**
Mohammed Shawagfeh

Models and Systems of Care

27 **Case Report: Victims of the Long Term Effects of Chemical Weapons on Health in Kurdistan of Iraq**
Kawa Dizaye

Research Article

35 **Acardia /Acephalic Twin Monster: Lessons for the Developing Countries**
Akinsanya, Olufemi, O, Loto, Olabisi, M

From the Editor

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This is the fourth issue this year with a good number of papers. A paper from Jordan aimed to evaluate if nasal synchronized intermittent mandatory ventilation is an effective initial mode of respiratory support for premature infants with respiratory distress syndrome. A total of 40 premature infants were studied, (21 males and 19 females) with gestational age ranging between 28 and 34 weeks (mean (SD) = 31.2 (2) weeks). The authors concluded that N-SIMV is a good and effective initial non-invasive ventilatory support for premature infants with mild to moderate RDS. It is safe, easy to use; requires minimal training, is not expensive and it can reduce the need for intubation. In the future N-SIMV might significantly reduce neonatal mortality and morbidity.

A paper from KSA looked at three cases of Heterozygous familial hypercholesterolemia (HeFH). It affects approximately 0.2% of people of European descent. Unfortunately there is no statistic in the Arab world to calculate the incidence or prevalence of this problem. It is a dominantly inherited condition and it is generally fully penetrated. Affected individuals always have LDL-C levels which are about double that of their unaffected siblings.

A paper from Nigeria reports a case of twin gestation (monochorionic diamniontic) in which one of the twins was acardiac, acephalic. His co twin suffered growth retardation and early neonatal death. Twin incidence in the Yoruba ethnic group is very high [6 per 100 births]; ironically this is the first report of acardiac monster in Nigeria if not in the African continent; only 8 percent of deliveries are conducted by doctors in Nigeria.

A paper from Iraq looked at Histological demonstration of Helicobacter Pylori (H Pylori) in patients with gastritis & peptic ulcer disease (PUD). The authors concluded that H. pylori infection in the stomach particularly in the antrum, causes a variety of histological changes. Immunohistochemistry was demonstrated to be the most accurate staining method for the histological detection of H. pylori compared with H&E modified Giemsa stains, and IgM serology. Modified Giemsa staining was shown to be more sensitive than H&E. Serum IgM testing was found to be of no much value.

A randomized, double-blind, prospective study was conducted at Prince Rashid Ben Al-Hassan military hospital, Irbid, Jordan, from June 2009 to July 2011. The aim was to evaluate the efficacy of intravenous magnesium sulphate on postoperative pain in abdominal surgery. The authors concluded that Preoperative magnesium sulphate infusion as an adjuvant analgesic reduced postoperative pain in patients undergoing major abdominal surgery and decreases requirement of rescue analgesia.

A paper from Iraq looked at VICTIMS OF THE LONG TERM EFFECTS OF CHEMICAL WEAPONS ON HEALTH IN KURDISTAN OF IRAQ. Extensive exposure to chemical weapons such as mustard gas, nerve gas and cyanide causes high mortality, morbidity, injuries, and chronic side effects in vital organs, especially the respiratory tract. Chemical weapons were heavily used by Iraq against Iranian soldiers between1984-1986, then, against the Iraqi Kurds during April 1987 and in Halabja on 18th March 1988. Reports suggested that as many as 2.9% of the Kurdish population have been exposed to chemical weapons at some level. The authors report on a case that describes a Kurdish lady who was exposed to mustard gas during a chemical attack in Sheikh Wasan in Iraq. The author stressed that this is one example of many of those who suffered from the effect of chemical weapons in Kurdistan of Iraq.

Case report: Heterozygous Familial Hypercholesterolemia (HeFH)

ABSTRACT

Heterozygous familial hypercholesterolemia (HeFH) affects approximately 0.2% of people of European descent. Unfortunately we have no statistics in the Arab world to calculate the incidence or prevalence of this problem. It is a dominantly inherited condition and it is generally fully penetrated. Affected individuals always have LDL-C levels which are about double that of their unaffected siblings. This is due to mutations of genes other than LDL receptors. Triglyceride levels are normal, but it could be the highly affected individual is obese. Interestingly, the typical HeFH patient may not in appearance conform at all to the clinician's concepts of a coronary-prone individual. We report three cases (3 cases) from one family having this condition and discuss the condition briefly.

Key words: **Low Density Lipoprotein, heterozygous familial hypercholesterolemia**

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Case Reports

We reported three cases of HeFH from one family (one girl, two boys). They are offspring of a woman and man suffering from dyslipidemia, DM, cardiac disease.

Miss A is 17 years old with normal developmental features. She is the daughter of Mrs D and Mr. F.

At the age of 15 years her mother took her to their family physician for an upper respiratory episode and routine checkup.

During examination no abnormal findings were detected except mild pharyngeal congestion and mild raised temperature which is consistent with upper respiratory tract infection. The family history of the patient was interesting. Her father was suffering from dyslipidemia since 10 years and also has diabetes type 2 with hypertension for the last 15 years as well as cardiac problems treated by surgical intervention. Her mother also is suffering from dyslipidaemia, hypertension and diabetes type 2. Both grandparents were suffering from dyslipidemia. Past medical history was not significant. Drug history was not significant. It was surprisingly that her lipid profile was abnormal. Her LDL-C was 7.2mmol.l and her T-Chol was 9mmol/l . Triglyceride was normal.

Patient was referred to a dietician for a structured diet program; after one month LDL-C did not decrease significantly and the patient was advised to start Statin (Atorvastatin 20mg/d). Her LDL-c started to improve and reached 3.1mmol/l .

The second case was the younger brother of Miss A. W is an eleven year old boy, and attends the family medicine clinic with his mother complaining of runny nose and sneezing which started 2 days ago mostly due to a common cold. The patient's family history was attached and the family physician raised the suspicion of familial hypercholesterolemia. Investigations were required. It was not surprising the lipid profile of the boy was abnormal. LDL-C was 3.8mmol/l

HDL-C was 0.98mmol/l, TG 1.75mmol/l and T-chol 5.62mmol/l. The diagnosis of familial hypercholesterolemia was discussed with the mother but she did not accept the idea of a new patient in the family. One year later the mother attended the clinic worried that her boy may develop a cardiac problem like his father and accepted to investigate the child again. The boy looked healthy and active. Examination did not show any significant findings. Lipid profile was requested and the results showed that LDL-C had become 4.8mmol/l, T-chol 6.4mmol/l, TG 1.33mmol/l and the HDL-chol 1.13mmol/l. The body mass index of the boy was within normal range for his age, weight and height.

The third case was a boy, 6 years old. D is the youngest brother of Miss A and W. He was accompanied by his mother and his brother in their consultation. The strong family history for familial hypercholesterolemia encourages the physician to discuss with the mother the importance of screening other siblings. The mother accepts the screening for D. Lipid profile was requested for the boy. The results showed that LDL-C was 3.9mmol/l and the T-chol was 5.9mmol, HDL-C was .96mmo/l and TG 1.13mmol.l. The diagnosis of familial hypercholesterolemia was raised and discussed with the mother.

Discussion

Familial hypercholesterolemia (FH) is an autosomal dominant disorder that causes severe elevations in total cholesterol and low-density lipoprotein cholesterol (LDL-C) (1-2).

Because FH is associated with a high risk for premature coronary artery disease (CAD), health professionals should be alert to the signs found during a physical examination and to the laboratory values suggestive of FH (3). Untreated men are likely to develop symptoms by the fourth decade of life. The onset of symptoms in women lags behind men by approximately 10-15 years. No accurate estimates of mortality rates are available. Children with heterozygous familial hypercholesterolemia (HeFH) do not have symptoms related to CHD.

Diagnostic criteria were available to help doctors to diagnose heterogeneous familial hypercholesterolemia (Box1) (Box 2).

Statistically, because the gene for FH is dominant, 50% of the patient's siblings will also have heterozygous FH. Screening is an important issue and it is cost effective intervention (Box 3).

Cholesterol deposition in non-vascular tissue is common, although heterozygous children do not usually have physical manifestations; adults do not invariably develop them. Corneal arcus is the most frequent finding, particularly in patients older than 30 years, but this finding is also common in older patients and African Americans without hypercholesterolemia. Xanthomas, most commonly of the Achilles tendon and extensor tendons of the hands, are rare in children and common in untreated adults.

Most children with He FH do not develop tendon xanthomas or corneal arcus. By the third decade of life, more than 60% of patients with untreated FH develop tendon xanthomas.

The figures in many textbooks suggest that tendon xanthomas in heterozygous patients are readily apparent upon gross inspection. Unfortunately, this often is not the case. Careful palpation rather than simple inspection may be necessary for detection of Achilles tendon xanthomas. A diffusely thickened tendon or one with discreet irregularities is suggestive of a xanthoma.

The diagnosis of heterozygous FH is based primarily on the finding of severe LDL-C elevations in the absence of secondary causes of hypercholesterolemia with triglyceride levels that are within the reference range or mildly elevated and HDL cholesterol (HDL-C) levels that are within the reference range or slightly low.

In patients with heterozygous FH, LDL-C levels are commonly higher than 250 mg/dL and usually increase with age. An LDL-C level higher than 200 mg/dL in a patient younger than 20 years is highly suggestive of HeFH. In adults, LDL-C levels higher than 290-300 mg/dL suggest heterozygous FH.

In patients with heterozygous FH, lifestyle modification should always be instituted but is unlikely to result in acceptable LDL-C levels; therefore, cholesterol-lowering medication (usually more than one) is necessary (4).

A diet that severely limits saturated fats, trans fats, and cholesterol is highly required for these patients (5). Usually patient needs referral to a qualified nutritionist to provide guidance in reducing intake of saturated and trans fats and cholesterol and assist in weight reduction if indicated. Desirable weight should be attained. Significant weight loss should improve all lipid parameters (LDL-C, HDL-C, triglycerides).

Aerobic and toning exercises improve blood lipid levels if performed for longer than 30 minutes, 4 or more days per week. While these efforts often have only a modest impact on LDL-C levels, rigorous dietary intervention works synergistically with lipid-lowering medications. Statins alone frequently do not lower these patients' cholesterol to therapeutic levels, and some patients are intolerant to statins. Combination or monotherapy with other current pharmacotherapies are options, but even with these some FH patients do not meet their low-density lipoprotein (LDL-C) cholesterol goals (6) (Box 4).

To approach the recommended LDL-C goals, a high dose of one of the 3 strongest HMG-CoA reductase inhibitors (statins), simvastatin, atorvastatin, or rosuvastatin, and one or more other LDL lowering medications, bile acid sequestrants, ezetimibe, or niacin, is recommended (7).

Aggressive cholesterol-lowering regimen can improve the lipid profile of FH (8) (Box 5).

To decrease the risk of myopathy, one step below the maximum dose of the statin should be considered. Because doubling the dose of any statin lowers the LDL-C only 6-7%, adding a second, third, or even fourth agent is more effective (9) .

If patients do not reach recommended treatment goals under the care of their primary care physicians, they should be referred to an endocrinologist or lipid specialist and to a qualified nutritionist.

a) Total cholesterol > 6.7 mmol/l or LDL cholesterol above 4.0 mmol/l in a child < 16 years or Total cholesterol >7.5 mmol/l or LDL cholesterol above 4.9 mmol/l in an adult. (Levels either pre-treatment or highest on treatment)

PLUS

b) Tendon xanthomas in patient, or in 1st degree relative (parent, sibling, child), or in 2nd degree relative (grandparent, uncle, aunt)

OR

c) DNA-based evidence of an LDL receptor mutation or familial defective apo B-100 Possible familial hypercholesterolaemia is defined as: a) above PLUS ONE OF d) or e)

d) Family history of myocardial infarction:

below age of 50 in 2nd degree relative or below age 60 in 1st degree relative

e) Family history of raised cholesterols:

>7.5 mmol/l in adult 1st or 2nd degree relative, or > 6.7 mmol/l in child or sibling under 16

Box 1: Diagnosis of FH (Simon Broome criteria)

(See Box 2: Dutch Lipid Network clinical criteria for diagnosis of heterozygous familial hypercholesterolemia (HeFH) next page)

The most cost effective screening strategy is to screen only the first degree relatives of identified FH patients (family screening).

Box 3: Screening of HeFH (10)

- Age > 10 years old if LDL-C levels remain above 5 mmol/L (190 mg/dL),
- LDL-c > 4 mmol/L (160 mg/dL) in the presence of a causative mutation, a family history of early cardiovascular disease or severe risk factors

Box 4: When to initiate pharmacological treatment (11)

- Reduce LDL-C by at least 30% between 10 and 14 years
- Reach LDL-C levels of less than 3.4 mmol/L (130 mg/dL) thereafter

Box 5: Objective of treatment (11)

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Box 1: Dutch Lipid Network clinical criteria for diagnosis of heterozygous familial hypercholesterolemia (HeFH)

Criteria	Points
1. Family history: a first-degree relative (a parent, offspring or sibling of the patient) with known	
a) Premature* coronary and vascular disease	1
b) Plasma LDL-C concentration > 95th percentile for age and sex	
i) In an adult relative	1
ii) In a relative < 18 years of age	2
c) Tendon xanthomata or arcus cornealis	2
2. Clinical history: patient has premature*	
a) Coronary artery disease	2
b) Cerebral or peripheral vascular disease	1
3. Physical examination of the patient	
a) Tendon xanthomata	6
b) Arcus cornealis in a patient < 45 years of age	4
4. LDL-C levels in patient's blood, mmol/L	
a) ≥ 8.5	8
b) 6.5-8.4	5
c) 5.0-6.4	3
d) 4.0-4.9	1
5. DNA analysis showing a functional mutation in the *LDLR* or other HeFH-related gene	8

Diagnosis	Total points
Definite HeFH	> 8
Probable HeFH	6-8
Possible HeFH	3-5

Note: LDL-C = low-density lipoprotein cholesterol.
*If a male relative, < 55 years of age; if a female relative, < 60 years.

Box 2: Dutch Lipid Network clinical criteria for diagnosis of heterozygous familial hypercholesterolemia (HeFH)

Histological demonstration of Helicobacter Pylori (H Pylori) in patients with gastritis and Peptic Ulcer Disease (PUD) in Sulaimani

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ABSTRACT

Background: H pylori infect one-half of the world population causing chronic gastritis, PUD and it has a role in the pathogenesis of gastric cancer and gastric lymphoma.

Aim of the study:

1. To determine whether immunohistochemical staining method used for histological identification of H pylori organisms is superior to H&E stain, modified Giemsa stain, and IgM serology.

2. To study the histological changes in the gastric mucosa due to H pylori infection using H&E and PAS stains.

3. To determine the relation of H. pylori infection with socio-demographic variables; age , sex, income, smoking and alcohol.

Setting: The laboratory of the departments of histopathology - College of Medicine, Sulaimani University and Shorsh Hospital and the Central Laboratory in Sulaimani.

Methods and Results: Histological sections from antral biopsies of 207 patients who underwent upper gastrointestinal endoscopy were examined histologically using H&E, modified Giemsa, and immunostains to identify H. pylori. The study showed that H. pylori infection causes histological changes including infiltration of the lamina propria with neutrophils, eosinophils and lymphocytes, glandular atrophy, intestinal metaplasia, presence of lymphoid follicles, and decreased mucous production. 124 cases (64.6%) were positive for H. pylori by immunohistochemical stain, 91 (47.4%) were positive by modified Giemsa stain, and 48 (25%) were positive by H&E stain. The present study showed that in single gastric biopsies, the immunohistochemistry is the most accurate staining method for the histological detection of H. pylori compared with H&E and modified Giemsa stains ($P < 0.001$).

The sensitivity of modified Giemsa was 73.3% which was more sensitive than H&E (38.7%). Negative predictive value for modified Giemsa and H&E stains were (67.3%), and (47.2%) respectively, the specificity and the positive predictive value was 100% for both. H. pylori infection was not associated with age, gender, alcohol consumption, and smoking. The prevalence of H. pylori infection was highest in the lowest social class 57.2%, lower in middle class 36.3% and lowest in the upper class (6.5%). This difference was significant ($P < 0.001$). For IgM serology only a subset (115) of the study group was used and for positive IHC results 88.2% of cases were serologically negative and 11.8% were positive. Eight of 73 females (11%) but none of 42 males, were positive. The sensitivity of IgM serology was 11.76%, negative predictive value was 43.9%, the specificity and positive predictive value was 100%.

Conclusion: H. pylori infection in the stomach particularly in the antrum causes a variety of histological changes. Immunohistochemistry was demonstrated to be the most accurate staining method for the histological detection of H. pylori compared with H&E modified Giemsa stains, and IgM serology. Modified Giemsa staining was shown to be more sensitive than H&E. Serum IgM testing was found to be of not much value.

Key words: H Pylori, Gastritis, peptic ulcer disease.

Introduction

H. pylori infection is a common infection worldwide, usually acquired in early childhood. Risk factors for H. pylori acquisition is age and poor socioeconomic status, where a high density of living, close contact with infected parents or numerous siblings and poor hygiene are common (Dondi et al., 2006)(1). Infection with H. pylori has been associated with an increased risk of PUD, gastric cancer and gastric lymphoma (Rothenbacher et al., 1998; Ma et al., 1998)(2). H. pylori infection can be diagnosed by invasive (endoscopic) and non-invasive (non-endoscopic) techniques (Ricci et al., 2007)(3). The invasive methods include gastroscopy with gastric mucosa biopsies for histologic examination, culture, polymerase chain reaction (PCR) or rapid urease test (RUT). The non-invasive methods include C13 urea breath test (C13-UBT), detection of antibodies in blood, urine, and saliva, and detection of H. pylori antigen in stool (Wu et al., 2006)(4). Histological examination of gastric mucosa can reveal the presence of the bacteria as well as the type of inflammation. Many stains can be used to detect the organism, for example Warthin-Starry, HP silver stain, Dieterle, Giemsa, Giminez, acridine orange, McMullen and immunostaining (Gatta et al., 2003; Ndip et al., 2003)(5,6). H. pylori can be visualized at high magnification with conventional hematoxylin and eosin (H&E) stained sections. H&E staining may be unreliable when few bacteria are present. In addition, luminal debris on the surface of the epithelium can be mistaken for H. pylori in H&E stained sections (Dunn et al., 1997)(7). Giemsa stain is most preferred because of its technical simplicity, high sensitivity and low cost (Gatta et al., 2003)5. Immunohistochemical staining has a high specificity and low interobserver variation (Jonkers et al., 1997)8, but it is expensive and may not be readily available in all pathology laboratories (Anim et al., 2000)(9).

Aims of the Study:

1. To determine whether immunohistochemical staining method used for histological identification of H pylori organisms is superior to H&E stain, modified Giemsa stain, and IgM serology.
2. To study the histological changes in the gastric mucosa due to H pylori infection using H&E and PAS stains.
3. To determine the relation of H. pylori infection with socio-demographic variables; age , sex, income, smoking and alcohol.

Materials and Methods

The 207 consecutive antral gastric specimens were obtained from 207 patients who had undergone upper GIT endoscopy in KCGH- Sulaimani-Iraqi Kurdistan, from July 2008-November 2008. As 15 biopsies were small and inconclusive, they were omitted.

At the same time blood samples were obtained from each patient for serological test in the Central Laboratory. Information regarding age, sex, previous drug history, history of alcohol consumption, smoking and income, were collected. Patients who had gastritis and peptic ulcer were included while those who were recently using proton pump inhibitors or antibiotics were excluded.

Results

Sex Distribution of Study Sample

The remaining 192 cases were included, with 115 females (59.9%) and 77 males (40.1%). There was no significant relationship between sex and H. pylori infection using H&E, modified Giemsa and IHC stains P= 0.67, 0.30, and 0.70, respectively. Using serology, 8 of 73 females (11%) but none of 42 males, were positive. This suggests a difference but chi-square value cannot be estimated because of absent data for males.

(See Table 1: Sex Distribution of H. Pylori Infection, opposite page)

Age distribution of the study sample is shown in Table 2.

Age (years)	Frequency	Percent
16-30	59	30.7
31-45	71	37.0
46-60	33	17.2
61-85	29	15.1

Table 2: Age Distribution of Study Sample

Age Distribution of H. Pylori Infection

The distributions of positive and negative immunohistochemical results by age were not statistically significant (P= 0.89).

(See Table 3: Age Distribution of H. Pylori Infected patients, opposite page)

Comparison of H&E, Modified Giemsa, IHC Stains and IgM Serology

68/ 192 patients (35.4%) were diagnosed as negative and 124 (64.6%) as positive for H. pylori by IHC, while 101 of 192 patients (52.6%) were diagnosed as negative and 91(47.4%) as positive for H. pylori by modified Giemsa stains. 144 of 192 patients (75%) were diagnosed as negative and 48 (25%) as positive for H. pylori by H&E, and 107 of 115 patients (93%) were diagnosed as negative and 8 (7%) as positive for H. pylori by IgM serology, as shown in Table 4 (page 10).

The differences between methods for demonstrating H. pylori infection is shown in Table 4 and Table 5. It was found that 124 cases were positive by IHC and 68 cases were negative. None of the cases that were negative by IHC were positive by IgM serology or by Giemsa or H&E stains. The number of positive IHC stains exceeded the positive results for Giemsa or H&E. For this reason, IHC was selected as the "gold standard" for H. Pylori infection. Of the 124 positive IHC results 33 (26.6%) were negative by Giemsa and 91 (73.4%) were positive; whereas, for H&E stains 76 (61.3%)

Variables	Sex		Pvalue
	Female N (%)	Male N (%)	
IHC			
Negative	42 (36.5)	26 (33.8)	0.70
Positive	73 (63.5)	51 (66.2)	
Giemsa			
Negative	57 (49.6)	44 (57.1)	0.30
Positive	58 (50.4)	33 (42.9)	
H&E			
Negative	85 (73.9)	59 (76.6)	0.67
Positive	30 (26.1)	18 (23.4)	
IgM Serology			
Negative	65 (89.0)	42 (100.0)	**N.A.**
Positive	8 (11.0)	0 (0.0)	

Table 1: Sex Distribution of H. Pylori Infection

Variables	Age (years)				Total	Pvalue
	16-30 N (%)	31-45 N (%)	46-60 N (%)	61-85 N (%)		
IHC						
Negative	23 (39.0)	25 (35.2)	11 (33.3)	9 (31.0)	68	0.89
Positive	36 (61.0)	46 (64.8)	22 (66.7)	20 (69.0)	124	
Giemsa						
Negative	31 (52.5)	38 (53.5)	18 (54.5)	14 (48.3)	101	0.96
Positive	28 (47.5%)	33 (46.5)	15 (45.5)	15 (51.7)	91	
H&E						
Negative	46 (78.0)	55 (77.5)	25 (75.8)	18 (62.1)	144	0.38
Positive	13 (22.0)	16 (22.5)	8 (24.2)	11 (37.9)	48	
IgM Serology						
Negative	39 (88.6)	34 (97.1)	20 (90.9)	14 (100.0)	107	0.33
Positive	5 (11.4)	1(2.9)	2 (9.1)	0 (0.0)	8	

Table 3: Age Distribution of H. Pylori Infected patients

were negative and 48 (38.7%) were positive. The differences between these modalities of testing are highly significant P< 0.001. For IgM serology, only a subset of the study group was used and for positive IHC results 88.2% of cases was serologically negative and 11.8% were positive. The sensitivity of IgM serology, modified Giemsa, and H&E was 11.76%, 73.3%, 38.7% respectively. The negative predictive value was 43.9%, 67.3%, 47.2%. The specificity and the positive predictive value was 100% for all. This is shown in Table 6 (next page).

Variables	Frequency	Percent	Total no.
IHC			
Negative	68	35.4	192
Positive	124	64.6	
Giemsa			
Negative	101	52.6	192
Positive	91	47.4	
H&E			
Negative	144	75.0	192
Positive	48	25.0	
IgM Serology			
Negative	107	93.0	115
Positive	8	7.0	

Table 4: The Number and Percentage of Positive and Negative Cases for H. pylori demonstrated by IHC, Modified Giemsa, H&E and IgM Serology

Tests	IHC	
	Negative N (%)	Positive N (%)
IgM Serology		
Negative	47 (100.0)	60 (88.2)
Positive	0 (0.0)	8 (11.8)
Giemsa		
Negative	68 (100.0)	33 (26.6)
Positive	0 (0.0)	91 (73.4)
H&E		
Negative	68 (100.0)	76 (61.3)
Positive	0 (0.0)	48 (38.7)

Table 5: Number and Percentage of Positive and Negative Cases for H. Pylori by IgM Serology, Modified Giemsa, and H&E Stains as compared With IHC

Types of tests	Sensitivity (%)	Specificity (%)	PPV (%)	NPP (%)
IgM Serology	11.76	100	100	43.9
Giemsa	73.3	100	100	67.3
H&E	38.7	100	100	47.2

Table 6: Sensitivity, Specificity, PPV, and NPP of IgM Serology, Modified Giemsa, and H&E Stains as compared to IHC

The differences in percentage of positive and negative cases of H. pylori infection diagnosed by H&E, modified Giemsa and IHC stains, and IgM serology are shown in Figure 3. It was found that 64.6% of cases were positive by IHC stain, 47.4% of cases were positive by modified Giemsa stains, and 25% of cases were positive by H&E stains. Only 7% of cases were positive by IgM serology.

Relation between H. Pylori Infection and Socioeconomic Status, Alcohol and Smoking

These distributions are shown in Table 8.

Socio-economic variables	Frequency	Percent
Income		
Low	86	44.8
Middle	76	39.6
High	30	15.6
Alcohol		
Positive	16	8.3
Negative	176	91.7
Smoking		
Positive	34	17.7
Negative	158	82.3

Table 7: The Number and Percentage of Cases according to Socioeconomic Status, Alcohol and Smoking

Socio-economic variables	Positive IHC (no. & percent)	Negative IHC (no.)	P value
Income			
Low	71 (57.2%)	15	**< 0.001**
Middle	45 (36.3%)	31	
High	8 (6.5%)	22	
Alcohol			
Positive	9 (7.3%)	7	0.65
Negative	115 (92.7)	61	
Smoking			
Positive	19 (15.3%)	15	0.33
Negative	105 (84.7%)	53	

Table 8: The Number and Percentage of Positive IHC Results according to Socioeconomic Status, Alcohol and Smoking

Histological Changes Due to Helicobacter Pylori Infection

1. Leukocyte Infiltration

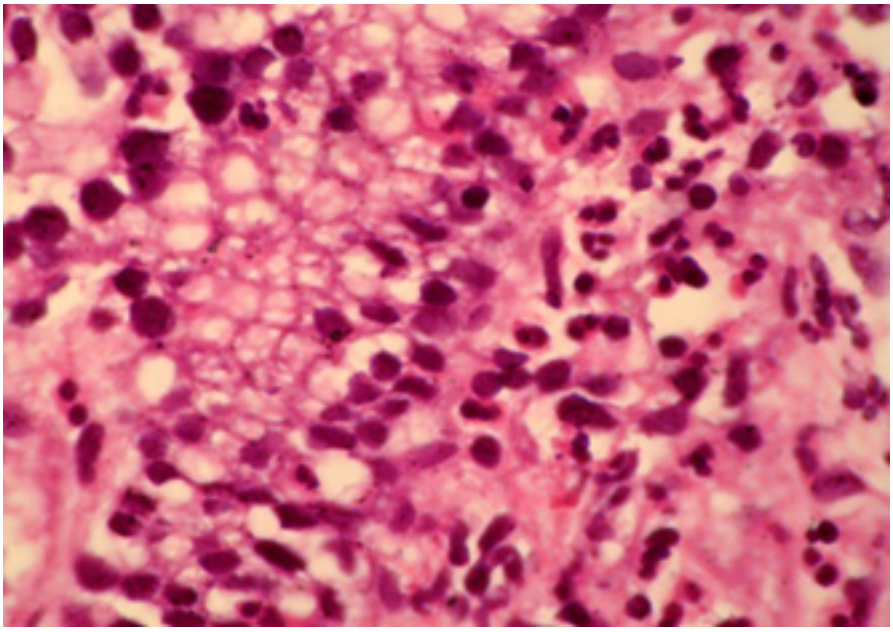

Plate 1: Section from Pyloric Antrum Showing Infiltration with Neutrophil (N), Eosinophil (E) and Lymphocyte (L) H&E Stains, 1000X.

2. Glandular atrophy

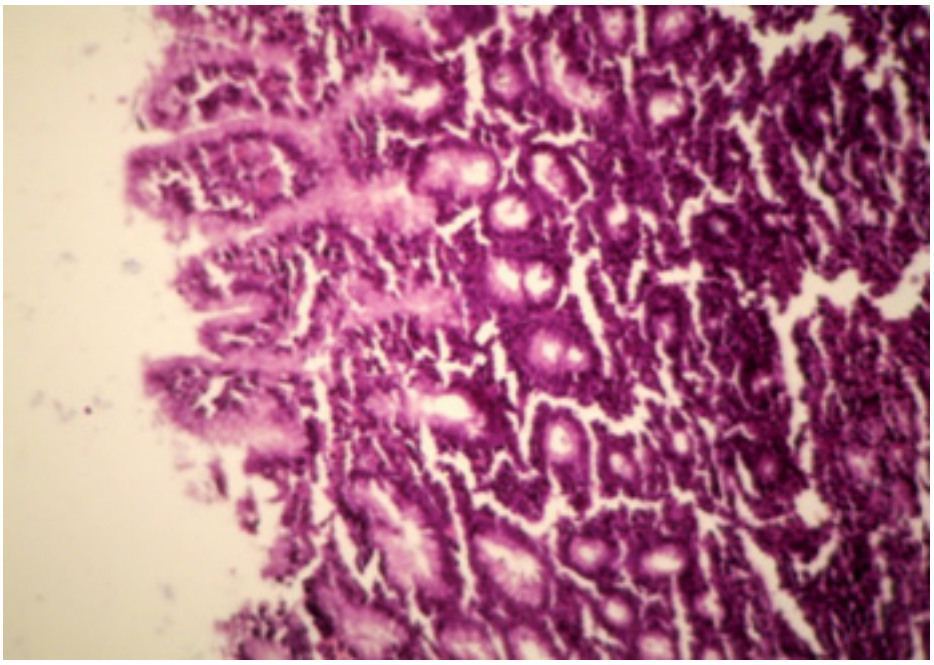

Plate 2: Section from Pyloric Antrum Showing Glandular Atrophy and Glandular Replacement by Fibrous Tissue H&E Stains, 400X.

3. Intestinal Metaplasia

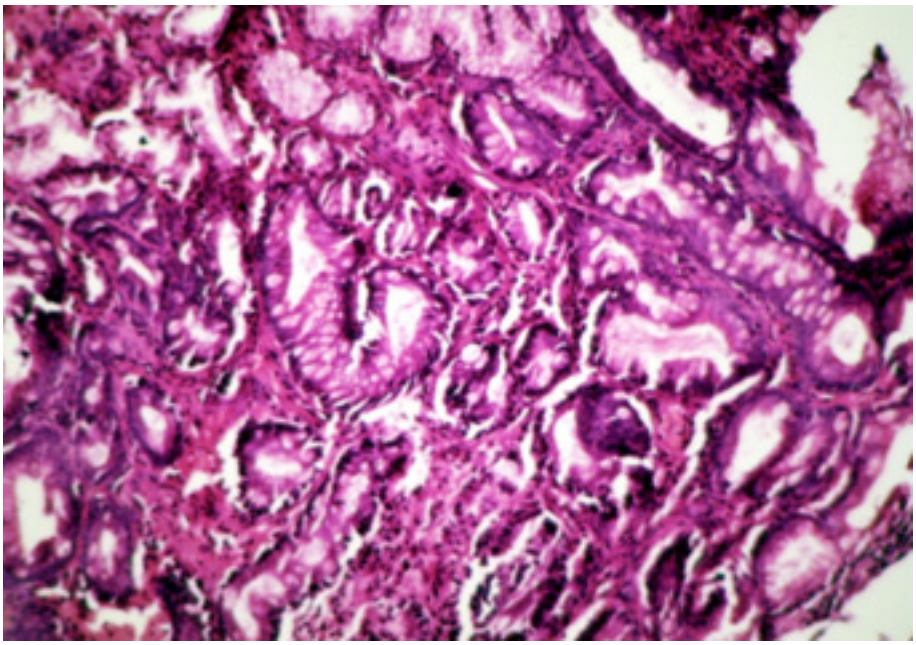

Plate 3: Section from Pyloric Antrum Showing Intestinal Metaplasia with Goblet Cells H&E Stains, 400X.

4. Lymphoid Follicles

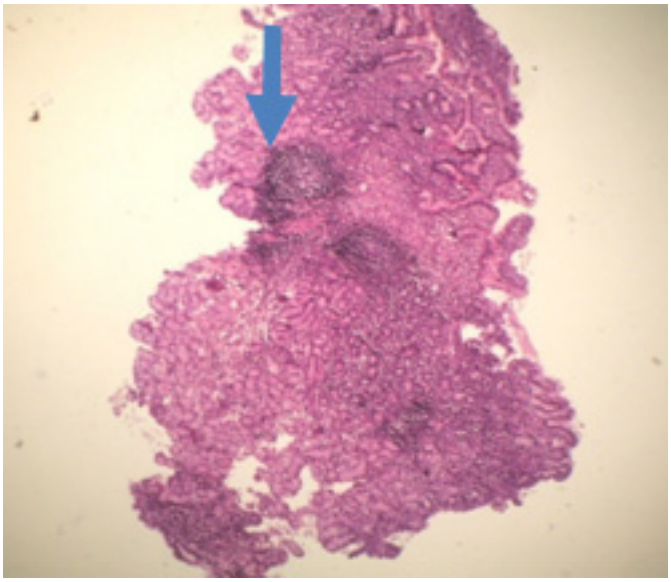

Plate 4: Section from Pyloric Antrum Showing a Lymphoid Follicle (Arrow). H&E Stains, 100X.

5. Histological Changes seen using PAS Staining Method

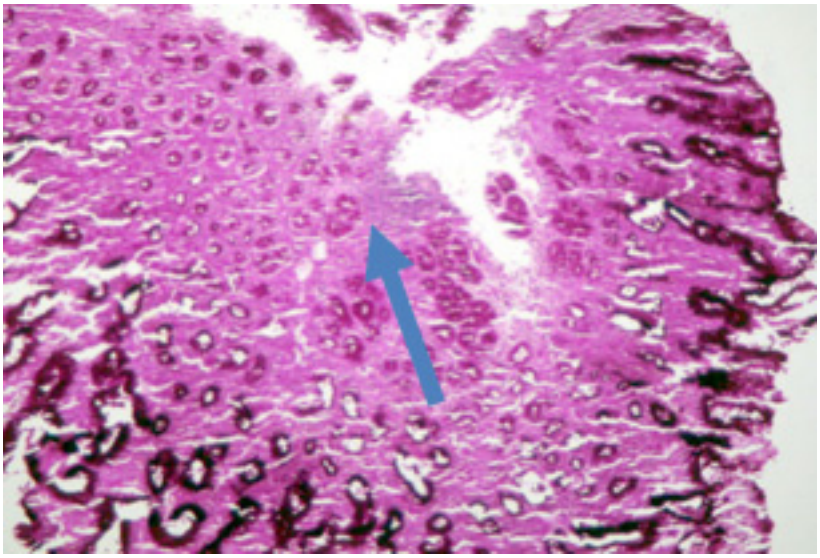

Plate 5: Section from Pyloric Antrum of H. Pylori Infected Patients Showing Decrease in Mucin in the Lower Antral Glands (Arrow). PAS Stain, 100X.

Demonstration of H. pylori Using H&E, Modified Giemsa and IHC Stains

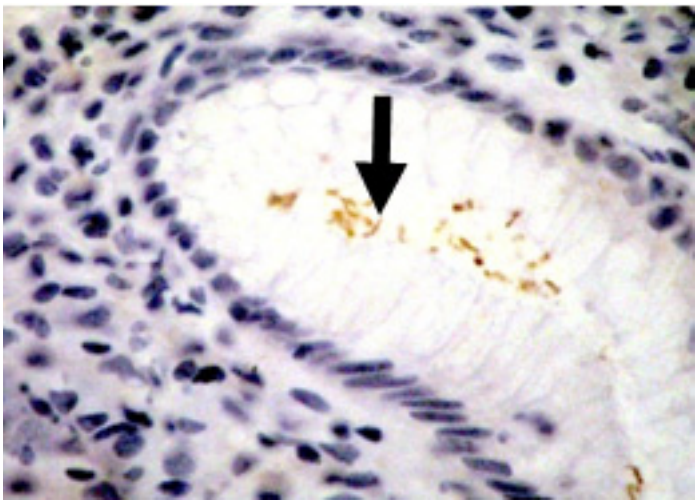

Plate 6: Section from Pyloric Antrum Showing Helicobacter Pylori (Arrow). Immunohistochemical Stain, 1000X.

Discussion

In this study, histological changes of H. pylori infection included infiltration of the lamina propria with neutrophils, eosinophils and lymphocytes, glandular atrophy, intestinal metaplasia, presence of lymphoid follicles, and decreased mucous production. Similar results had been reported by Toulaymat et al. in 1999(10), Turkay(11), Stolte and Eidt (12), in 1992& Dixon et al., in 1996(13).

In this study, three stains, H&E, modified Giemsa, and immunohistochemical stains were used for the detection of Helicobacter pylori in antral biopsies. The results showed that 124 cases (64.6%) were positive by immunohistochemical stains, 91 cases (47.4%) were positive by modified Giemsa stains, and 48 cases (25%) were positive by H&E stains. The present study showed that in single gastric biopsies immunohistochemistry is the most accurate staining method for the histological detection of H. pylori compared with H&E and modified Giemsa stains ($P < 0.001$).

The results were in agreement with that reported by Ashton-Key et al. (1996)(14) , Babic et al., Basic et al. (2002)(15), Loffeld et al. (1991)(16), Orhan et al. (2008)(17), but contradict with that obtained by Anim et al. (2000)(9).

In the present study, the sensitivity of modified Giemsa was 73.3% which was more sensitive than H&E at 38.7%. The negative predictive value for modified Giemsa and H&E stains were 67.3% and 47.2% respectively. The specificity and the positive predictive value was 100% for both. The results of the present study differed with that obtained by Laine et al. (1997)(18), Wabinga (2002)(19) & Jonkers et al.(8) (1997) The difference would indicate that Jonkers et al. (1997) had a large number of false positive Giemsa stains while in the current study there were no false positive Giemsa results when compared to the gold standard of immunohistochemistry.

Regarding the relationship between sex and H. pylori infection, in this study there was no significant relationship between sex and H. pylori infection using H&E, modified Giemsa and immunohistochemistry. This is in agreement with Megraud et al. (20), Zaterka et al. (21); Lin et al. (22),but in contrast Naja et al. (23) found that men have significantly higher infection rates than women.

In the present study patients are classified according to their age into four groups (16-30, 31-45, 46-60, and 61-85 years old). The proportion of positive cases diagnosed by immunohistochemistry increased slightly but not significantly with increasing age from 61.0% in the age group 16-30 years, followed by 64.8% in the age group 31-45 years, 66.7% in the age group 46-60 years, and 69.0% in the age group 61-85 years. Zaterka et al. (21), Khan and Ghazi (24), Ahmed et al. (25), found a positive association with aging, and Murray et al. (26) found that the prevalence of infection increased from 23.4% in 12-14 years old to 72.7% in 60-64 years old.

Regarding the relationship between H. pylori infection and socioeconomic status, in this study, it was found that the prevalence of H. pylori infection was highest in the lowest social class of 57.2%, lower in middle class at 36.3% and lowest in the upper class at 6.5%. This difference was significant $P < 0.001$. The results of the present study were in agreement with Sitas et al. (27), Zaterka et al. (21)

The present study showed no significant association between H. pylori infection and smoking. These results agreed with Graham et al (28), Zaterka et al. (21), and EUROGAST (29).

In this study it was found that there was no significant association between H. pylori infection and alcohol consumption. These results agreed with Eurogast (29), Kuepper-Nybelen et al (30), Graham et al. (28) and Zaterka et al. (21)

For IgM serology, only a subset of the study group was used and for patients with positive IHC results 88.2% were serologically negative and 11.8% were positive. Eight of 73 females (11%) but none of 42 males were positive. This suggests a difference, but a chi-square probability could not be estimated because of the empty data for males. The sensitivity of IgM serology was 11.76%, the negative predictive value 43.9% and the specificity and positive predictive value 100%. These results agreed with that

obtained by Andersen et al. (31), and Blecker et al. (32). The low value of 11% positive IgM serology found in the current study indicates that the test is of little value in detecting acute infection. Andersen et al. (31) also found that few patients (4.5%) had increased levels of IgM antibodies to H. pylori which again indicates the inefficiency of the test.

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Nasal SIMV as an initial mode of respiratory support for premature infants with RDS. An observational study

ABSTRACT

Objective: **This study aimed to evaluate if nasal synchronized intermittent mandatory ventilation is an effective initial mode of respiratory support for premature infants with respiratory distress syndrome.**

Method: **Forty premature infants born at gestational age 28-34 week with RDS diagnosed by chest x-ray and clinical Downes score were connected through a nasal cannula to respirator using the SIMV mode immediately after birth. Arterial blood gases taken before N-SIMV then after two hours of N-SIMV and then every twelve hours, a daily chest x- ray and a daily clinical evaluation by the attending neonatologist throughout the period of the study.**

Results: **A total of 40 premature infants (21 males and 19 females) with gestational age ranging between 28 and 34 weeks (mean (SD) = 31.2 (2) weeks). Their birth weight ranged between 0.880 and 2.0 kg with a mean (SD) of 1.49 (0.5) kg. N-SIMV was associated with almost ideal physiological arterial carbon dioxide tension, PaO2, pH and HCO3 (mean Pa CO2 = 37.5 mm.Hg, mean PaO2 = 82.5mm.Hg, mean O2 sat. = 95 %, mean pH = 7.32 and mean HCO3 = 19.5 mmol/l). Only 3 (7.5%) infants developed apnea. Only one premature infant developed collapse consolidation of the right upper lobe that responded to positional therapy and blood culture was positive in one preterm infant = 2.5 % of infants included in the study. Neither gastrointestinal perforation nor abdominal distention were reported in preterm infants included in the study during N-SIMV support. N-SIMV is associated with relatively very low incidence of BPD = 2.5 % of all preterm infants included in the study (one infant developed BPD). N-SIMV failure was defined per our protocol = 3/40 (7.5 %).**

Conclusion: **N-SIMV is a good and effective initial non-invasive ventilatory support for premature infants with mild to moderate RDS. It is safe, easy to use; requires minimal training, is not expensive and it can reduce the need for intubation In the future N-SIMV might significantly reduce neonatal mortality and morbidity.**

Key words: **premature newborn, surfactant, nasal ventilation, non-invasive ventilation and bronchopulmonary dysplasia.**

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Introduction

The commonest respiratory problem of premature infants is respiratory distress syndrome (RDS) that is caused by immature lungs and surfactant deficiency (1). RDS could be treated with exogenous surfactant and by increasing the functional residual capacity (FRC) with continuous positive airway pressure (CPAP) support (2). Since the introduction of mechanical ventilation through endotracheal tube in the 1960s, survival of premature infants improved but morbidity remained high and high rates of air leak were reported (3). A significant morbidity in preterm infants is bronchopulmonary dysplasia (PBD), the incidence which correlates with the use of mechanical ventilation (4,5).

Nasal respiratory support (NRS) is a noninvasive method that includes N-CPAP and nasal ventilation-(N-IPPV, N-SIMVand nasopharyngeal). In1971 George Gregory first described the use of continuous positive airway pressure (CPAP) as early treatment of respiratory distress syndrome (RDS). In general even N-CPAP has been shown to be an effective option in RDS treatment that reduces the need for invasive mechanical ventilation(6), but it still has many disadvantages that include nasal bone destruction (7), pneumothorax (3), abdominal distention, CO2 retention and N-CPAP failure. Post extubation use of N-SIMV was found to be a very effective mode of respiratory support and associated with increased tidal volume and minute volume, much more stable chest wall and less work of breathing in premature infants compared with N-CPAP (8,9). We hypothesize that N-SIMV can be an effective initial respiratory support in premature infants with RDS that are associated with few complications. The objective of this observational study was to evaluate if nasal synchronized intermittent mandatory ventilation (N-SIMV) is an effective initial mode of respiratory support for premature infants with respiratory distress syndrome.

Methods and Patients

This is a 6-month observational study that took place between January 2011 and June 2011 at the level III NICU at Prince Hashem Ben Al- Hussein Military Hospital, North of Jordan. A total of 40 premature infants born at gestational age of 28-34 weeks, and with birth weights between 880 and 2000 g with RDS diagnosed by chest x-ray and clinical Downes score (4-8) points were eligible to be enrolled in this study. Infants with respiratory arrest, Downes score of more than 8 points, nasal obstruction and facial malformation were excluded from the study. Downes score was estimated and arterial blood gases (ABGs) were taken while the premature infant was on low flow nasal cannula 1.5 l/min, immediately before connection of the premature infant with RDS to SIMV machine (BEAR CUB 750 VS, Sensor Medics or Neoport E100M infant ventilator) with built in synchronization device through binasal short prongs using 2.5 ET tube adaptors.

Surfactant as clinically indicated was given using the two hours Intubation Surfactant Extubation approach. ABGs were taken before N-SIMV and then after two hours of N-SIMV and then every twelve hours using the inserted umbilical artery catheter, and a daily CXR done throughout the period of the study. Suggested settings of respirator were as follows : Rate = 15 -18 / min (preferably 12) and was adjusted according to Pco2, PIP = 5 - 12 cm H2 0 (preferably 12), PEEP = 0 - 6 (preferably 6), FiO2 = 40 % but was adjusted to maintain oxygen saturations 90 to 96% on pulse oximetry , Ti = 0.3 - 0.5 seconds, and Fl = 8 ml/ min. N-SIMV failure was considered if one of the following were met: pH < 7.24, Pco2 > 60 mm.Hg, need for FiO2 = 1.0, 2-3 apnoeas/ bradycardias per hour, and any apnoea needing mechanical ventilation. Discontinuation of N-SIMV was allowed to only oxygen or low flow nasal cannula of < 1 L/ min when on FiO2 of = 21%, with normal ABGs and with no respiratory distress or apnoea. Infants included in the study were monitored as per standard NICU nursing protocols, rounded and medically managed by the attending neonatologist on a daily basis. ABGs were taken by a Registered Nurse, data was collected by the neonatal fellow, and respiratory machine setting was checked by the respiratory therapist. To train the staff on connecting the premature infant to the N-SIMV, three sessions were conducted by the research team. Data were analyzed using the Statistical Package for Social Sciences version 15. Ethical approval was taken from Jordanian Royal Medical Services ethical committee.

Results

A total of 40 premature infants (21 males and 19 females) with gestational age ranging between 28 and 34 weeks (mean (SD) = 31.2 (2) weeks). Their birth weight ranged between 0.880 and 2.0 kg with a mean (SD) of 1.49 (0.5) kg. (Table -1).

Figures 1 and 2 show the changes in PaO2 and PaCO2 over time. PaO2 increased after the initiation N-SIMV and reached the physiological level within 24 hours of initiation, after which it continued to increase. On the other hand, PaCO2 stared to decrease immediately after the initiation of N-SIMV and reached the physiological level after maximum 12 hours, after which it continued to decrease. The linear changes in PaO2 and PaCO2 after the N-SIMV initiation were significant

Demographics	n = 40
Mean gestational age ± SD	31.2± 2
Birth weight (kg)	1.49± 0.5
Male : female	21 : 19
Maternal dexamethasone :-	
- None	13 (32.5 %)
- 1 dose	9 (22.5%)
- 2 doses	18 (45 %)
Downes score (points)	5 ± 2
Surfactant :-	
- None	32 (80 %)
- 1 dose	2 (5 %)
- 2 doses	6 (15 %)

Table 1: Characteristics of premature infants included in the study

(P<0.05). After N-SIMV initiation O2 saturation increased from 85% to 95% within 12 hours. After that, O2 saturation fluctuated between 94% and 97% over time.

As evidenced by CXR, N-SIMV did not cause lung hyperinflation and none of the infants developed pneumothorax. Only 3 (7.5%) infants developed apnea. None of them responded to simple intervention. The three infants with apnea needed aminophyllin and only one needed intubation. Only one premature infant developed collapse consolidation of the right upper lobe that responded to positional therapy. Blood culture was positive in one preterm infant and one developed late sepsis. Only one infant died on day 14 of life due to intestinal obstruction. Neither gastrointestinal perforation nor abdominal distention was reported in preterm infants. Of all preterm infants, only one infant developed BPD (which was defined by need of supplemental O2 for the first 28 days of life). (Table 3, page 21).

N-SIMV failed in three patients. Of those, one was < 29 week gestation, one with birth weight < 1000 grams, and one was with severe apnea that required intubation. Two of them were preterm infants with Down's score of more than 6 points. All

	PaO2 mm.Hg	PaCO2 mm.Hg	PH	O2 SAT %	HCO3 Mmol/L
Before nasal SIMV	61.9	54.7	7.20	85%	13.5
2 hrs	69.81	47.2	7.20	91%	15.0
12 hrs	73.95	45.4	7.20	95%	15.0
24hrs	74.5	42.0	7.25	94%	16.7
36hrs	80.7	38.3	7.30	94%	18.6
48hrs	85.4	34.8	7.30	95%	19.8
60hrs	86.8	34.9	7.30	94%	20.8
72hrs	90.2	32.5	7.30	95%	21.3
84hrs	87.3	31.0	7.40	96%	21.5
96hrs	90.0	33.0	7.40	97%	20.4
108hrs	94.0	29.0	7.40	97%	22.0

Table 2: Mean results of ABGs

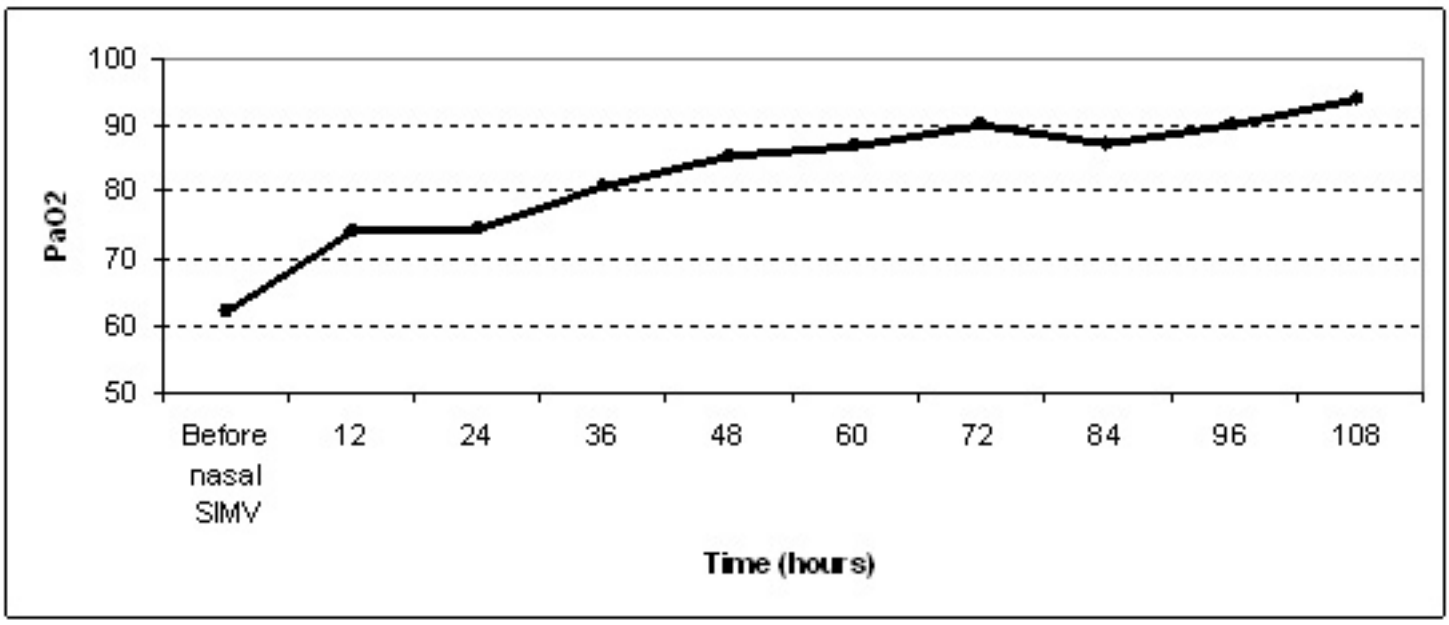

Figure 1: Changes in PaO2 (mm.Hg) over time (hour)

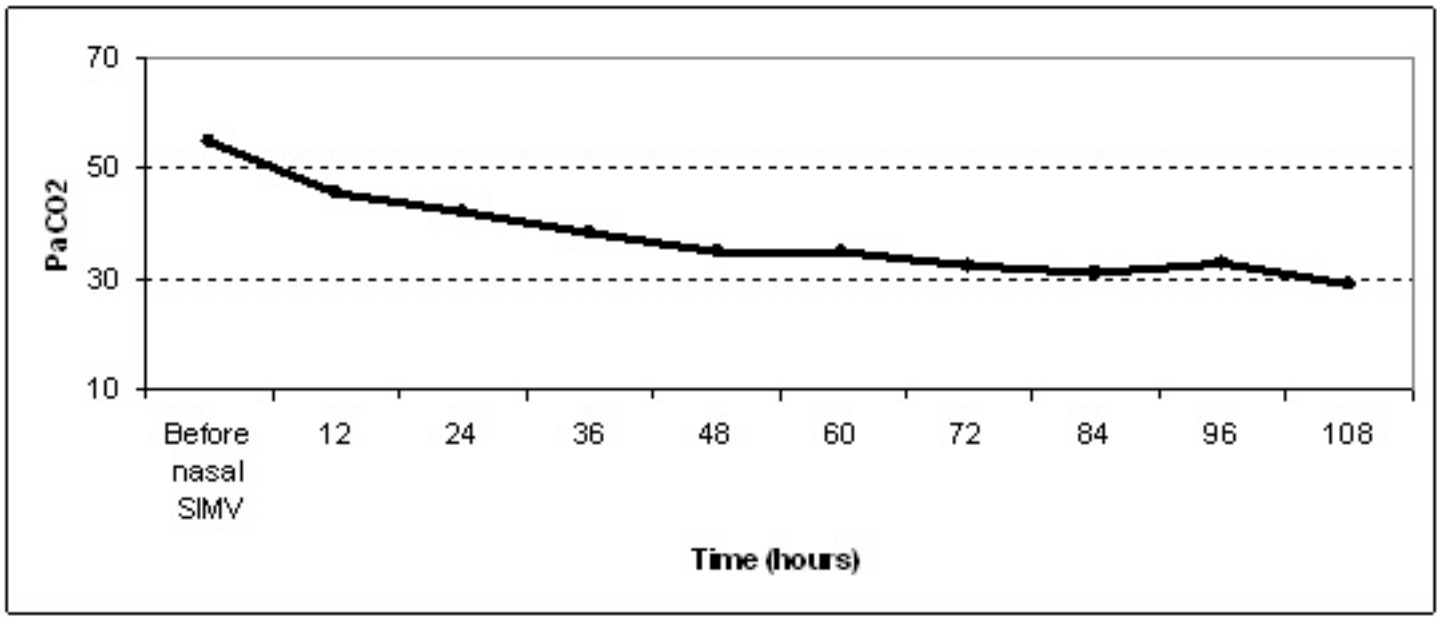

Figure 2: Changes in PaCO2 (mm.Hg) over time (hour)

infants who failed N-SIMV received Servanta. (Table 3). The duration of N-SIMV support ranged between 2.5 and 4 days for preterm infants.

Analyzing the results of ABGs taken during the study we found that using N-SIMV was associated with almost ideal physiological arterial carbon dioxide tension, PaO2, pH and HCO3 (mean Pa CO2 = 37.5 mm.Hg , mean PaO2 = 82.5 mm.Hg, mean O2 sat. = 95 %, mean pH = 7.32 and mean HCO3 = 19.5 mmol/l). (Table -2).(Figure- 2). (Figure 1).

Discussion

RDS is a multi-factorial entity caused by immature lungs, surfactant deficiency, chest wall instability, poor central respiratory drive and upper airway obstruction (1,10). With increased survival of very low birth weight and extremely low birth weight infants, there is an increasing effort to use non-invasive ventilation to minimize the need for prolonged invasive mechanical ventilation to reduce ventilator-induced lung injury, air leak and oxygen toxicity (11).

Many studies have compared the efficacy of post extubation use of N-CPAP, nasal intermittent positive pressure ventilation (N-IPPV) and N-SIMV (8, 9,10) and few studies have assessed the efficacy of N-IPPV (12,13) and nasopharyngeal -SIMV (14) as initial respiratory support in RDS preterm infants but to the best of our knowledge this is the first observational study of primary mode N-SIMV as initial respiratory support in premature infants with RDS, not only in Jordan and the region, but in the world.

During the study we found that to train the staff on connecting the premature infant to the N-SIMV needed approximately not more than ten minutes and the time needed to connect the baby to the system ranging between one and a half to two minutes.

Studying the results of ABGs we found that using N-SIMV we can have almost ideal physiological arterial carbon dioxide tension, pH and HCO3 (mean Pa CO2 = 37.5 mm.Hg, mean PaO2 = 82.5mm.Hg , mean O2 sat. = 95 %, mean pH = 7.32 and mean HCO3 = 19.5mmol/l). That can't be reached using any other non-invasive respiratory method especially the N-CPAP as it is well known to be frequently associated with CO2 retention and respiratory acidosis. Our study showed that synchronizing N-SIMV inflations with an infant's own breaths is not associated with the occurrence of air leak like invasive and especially other non invasive (N-CPAP and N-IPPV) modes of ventilation that can deliver high pressure during spontaneous expiration, increasing the risk of raised upper airway pressure and pneumothorax; (15,16) more than that in our study we showed that N-SIMV does not cause lung hyperinflation as evidenced by CXR and thus decreases the incidence of air leak syndrome and might not be associated with increased pulmonary blood flow with a subsequent increase in pulmonary vascular resistance and decrease in cardiac output.

A controlled study of unsynchronized nasal intermittent mandatory ventilation done by Ryan CA et al (1989) showed no advantages in the treatment of apnea of prematurity (17), but a study by Neil N. Finer et al (9) has confirmed that post extubation N-SIMV use has a therapeutic effect in decreasing apnea. Our findings support those of Neil N. Finer et al and show that N-SIMV is associated with low prevalence of apnea (infants who developed apnea = 3/40 (7.5 %) of the total infants included in the study. Low incidence of apnea during N-SIMV can be explained by the fact that the upper airway of the preterm infant is very compliant and therefore prone to collapse thus using N-SIMV not only splints the upper airway reducing obstruction and apnea but also helps the lung to expand and prevents alveolar collapse. It is a well known fact that invasive mechanical ventilation is usually associated with high incidence of secondary chest infection and sepsis. In our study only one premature infant (2.5 %) developed collapse consolidation of the right upper lobe that responded

Complication	Number of newborns n = 40	percentage
Apnea :	3	7.5%
-Apnea responded to minimal intervention	0 of 3	0.0%
-Apnea needed aminophyllin	3 of 3	100% of total infants who developed apnea
-Apnea needed intubation	1 of 3	33.3% of total infants who developed apnea
Need for intubation (N-SIMV failure):	3	7.5%
- Gestational Age < 29 weeks	2 of 3	66.6%
- B.Wt < 1000 g	1 of 3	33.3%
- Apnea	1 of 3	33.3%
- Downes score > 6	2 of 3	66.6%
- Hx of maternal dexamethazone	0 of 3	0.0%
- Hx of surfactant	3 of 3	100%
Duration of N-SIMV (days)	3.1	
Nasal destruction	0	0.0%
Abdominal distention vs intestinal perforation	0	0.0%
Air leak	0	0.0%
Bronchopulmonary dysplasia	1	2.5%
Early sepsis	0	0.0%
Late sepsis*	1	2.5%
Chest infection	1	2.5%
Interventricular hemorrhage	0	0.0%
Death**	1	2.5%

*klebsiella; ** due to intestinal obstruction

Table:3: Complications of N-SIMV

to positional therapy and blood culture was positive in 1/40 (2.5 %) of infants included in the study.

In our study and due to the short time needed for N-SIMV support and that we used a nasal cannula that can be easy fixed to the infant nose and face causing no pressure on the nose, therefore not only was there no single case of nasal bone destruction but also no case of nasal soft tissue injury was reported.

Uncontrolled studies N-SIMV suggested that occasional gastrointestinal perforation could occur (18), but in our study neither gastrointestinal perforation nor abdominal distention were reported.

Multiple factors contribute to BPD (volutrauma, barotrauma and atelectasis or end-expiratory alveolar collapse) but intubation and mechanical ventilation of preterm infants is the single most important predictor of subsequent BPD (19). Our study used the non-invasive N-SIMV associated with relatively very low incidence of BPD = 2.5 % of all preterm infants included in the study (one infant developed BPD). Of note the high percentage, 2.5, is due to small total number of premature infants included in the study. Here we want to stress that we used Fi02 < 40 % most of the time and the mean duration of nasal O2 supplementation was 3.1 days which can explain the low occurrence of BPD in our study.

N-SIMV failure as defined per our protocol = 3/40 (7.5 %) of them 1/3 (33.3 %) are premature of < 29 GA , 1/3 (33.3 %) of birth weight < 1000 grams and 1/3 (33.3 %) with severe apnea required intubation, which could mean that extremely premature infants and preterm infants with extremely low birth weight and those with Downes score of more than 6 points are not responding well to N-SIMV.

Our study has some limitations. The major limitations are lack of a comparison group, the sample size, and difficulty obtaining consent in a timely manner, lack of residents' time, especially during night duties and that it was not designed to evaluate long-term outcomes. But we still hope that this new approach to respiratory assistance in preterm newborns with RDS will significantly reduce neonatal morbidity and will reduce the iatrogenic complications of neonatal intensive care and stimulate additional prospective evaluations of this approach.

Conclusion

We conclude that N-SIMV is a good and effective initial non-invasive ventilatory support for premature infants with mild to moderate RDS. It is safe easy to use, requires minimal training, is not expensive and it can reduce the need for intubation. In the future N-SIMV might significantly reduce neonatal mortality and morbidity.

Evaluation of long-term pulmonary and neuro-developmental outcomes of N-SIMV use justify the need for more trials comparing different techniques of respiratory support. To determine the optimal settings for N- SIMV to establish best practice, further research is required.

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Efficacy of intravenous magnesium sulphate on postoperative pain

ABSTRACT

Objectives: To evaluate the efficacy of intravenous magnesium sulphate on postoperative pain in abdominal surgery.

Methods: A randomized, double-blind, prospective study was conducted at Prince Rashid Ben Al-Hassan military hospital, Irbid, Jordan, from June 2009 to July 2011. Two hundred patients undergoing abdominal surgery were divided randomly into two groups of 100 each. Group-I received magnesium sulphate while Group-II received the same volume of isotonic sodium.

Results: Pain in the postop period was significantly lower in the magnesium sulphate group in comparison to the control group as the visual analogue scale (VAS) score was recorded at emergence from anaesthesia and at 2, 12, and 24 hours after the surgery. Rescue analgesia requirement postoperatively in the first hours in the recovery room and during 24 hours was significantly lower in patients of group-I than in group-II.

Conclusion: Preoperative magnesium sulphate infusion as an adjuvant analgesic reduced postoperative pain in patients undergoing major abdominal surgery and decreases requirement of rescue analgesia.

Key words: Intravenous magnesium sulphate, postoperative pain, abdominal surgery.

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Introduction

Magnesium sulphate is a chemical compound containing magnesium, sulfur and oxygen, with the formula MgSO4, and it is the fourth most common cation in the body which has numerous physiological activities including activation of many enzymes involved in energy metabolism and protein synthesis(1).

Magnesium (Mg) is a non-competitive N-methyl-d-aspartate (NMDA) receptor antagonist with antinociceptive effects and it has been suggested that magnesium has the potential to treat and prevent pain by acting as an antagonist of N-methyl-D-aspartate (NMDA) receptors(2). Also it has been widely used as a tocolytic agent and an anticonvulsant for the treatment of preterm labour(3) and pre-eclampsia(4), respectively. On the other hand, magnesium sulphate has been previously investigated as a possible adjuvant for intra- and post-operative analgesia. The majority of these studies suggest that perioperative magnesium sulphate reduces anaesthetic requirements, improves postoperative analgesia(5), and shortens anaesthetic induction by propofol(6). However, some studies have concluded that magnesium sulphate has limited(7) or no effect(8).

Since in literature there is no convincing evidence to support analgesic efficacy of magnesium sulphate, various studies have been done regarding the role of magnesium sulphate in postoperative analgesia(9,10), but there are only a few studies in our country addressing this issue, so in this study we planned to study the role of magnesium sulphate for postoperative analgesia in our area, in patients attending this hospital in the north of Jordan.

Methods

This randomized, double-blind, prospective study was undertaken to evaluate the effects of magnesium sulphate on anaesthetic requirements and postoperative analgesia in patients undergoing abdominal surgery. The study was conducted at Prince Rashid Ben Al-Hassan military hospital in the north of Jordan, from June 2009 to July 2010 after ethics committee approval. Two hundred patients undergoing abdominal surgery were randomly assigned to one of the two groups divided into 100 each. Preoperative anesthesia was the same for both groups. The patients of the magnesium

sulphate group (Group-I) received magnesium sulphate 50 mg/kg in 200 ml of isotonic sodium chloride solution IV whereas patients in the control group (Group-II) received the same volume of isotonic sodium chloride over 30 minutes preoperatively.

Randomization and sample population were derived by using computer-generated Microsoft Excel programme. The purpose, protocol of study and use of visual analogue scale (VAS) was explained to patients and written informed consent was obtained from all patients. Exclusion criteria were the following: those with impaired renal or hepatic function, varying degree of heart blocks, hypertension, diabetes, neurological disorders, myopathy, allergy to magnesium sulphate, drugs or alcohol abuse, and pregnant women.

Pain at emergence from anaesthesia and 2, 12 and 24 hours after surgery was evaluated using a 0-10 cm VAS (0 - No pain at all to 10 - Worst pain imaginable). The timing and dosage of rescue analgesic during the first 24 hours after operation, was noted. All the data were compiled and continuous variables were analyzed using Student t-test.

Results

The two groups were comparable with respect to age, weight, gender, duration of anesthesia and duration of surgery of patients. Comparison of haemodynamic paremeters (mean arterial pressure and heart rate) during study medication and intraoperative period between group I and group II at different time intervals, was statistically insignificant. The incidences of PONV (Nausea and vomiting) and shivering after surgery was statistically similar in both groups during the intraoperative as well as in the postoperative period.

Pain scores were evaluated using a 0-10 cm Visual Analogue Scale (VAS), starting from 0, no pain, to 10, worst pain imaginable). The VAS score was recorded at emergence from anaesthesia and at 2, 12, and 24 hours after the surgery. Table I shows that at different time intervals patients in group I had less pain than in group II when compared on VAS ($P<0.05$), except at emergence of anaesthesia ($P>0.05$).

During the first hour the patients were kept in the recovery room then transferred to the surgical ward and rescue analgesia was provided at VAS>3 in the form of pethidine 0.5

Visual analogue scale	Group I (Mean±SD)	Group II (Mean±SD)	P value
Emergence from anaesthesia	1.48±0.6	1.58±0.4	0.137
After 2 hours	1.21± 0.73	1.77±0.33	0.000
After 12 hours	2.52±1.31	3.62±1.42	0.000
After 24 hours	0.56±0.64	1.10±0.24	0.000

P<0.05 significant, P>0.05 insignificant.

Table 1: Assessment of pain (visual analogue scale) in post-operative period

Discussion

Magnesium is the fourth most plentiful cation in the body and the second most plentiful intracellular cation after potassium. As magnesium blocks the N-methyl-D-aspartate receptor and its associated ion channels, it can prevent central sensitization caused by peripheral nociceptive stimulation. Magnesium also has antinociceptive effects in animal and human models of pain(11).

We confirmed in this study our hypothesis that magnesium sulphate (50 mg/kg) infusion given before induction of anaesthesia, decreases postoperative pain in patients undergoing major abdominal surgery. Consequently, patients in the control group required analgesics earlier and required greater doses to achieve satisfactory analgesia. Interestingly, this increased pethidine consumption.

Many authors have studied the role of magnesium sulfate for postoperative analgesia and agree with our results. Koinig H et al(12) have performed a randomized, double blind study; and they conclude that the perioperative administration of i.v. magnesium sulfate reduces intra- and post-operative analgesic requirements in patients with almost identical levels of surgical stimulus. Also Lee DH et al(13) found in his study that magnesium sulphate can be recommended as an adjuvant during general anaesthesia for Caesarean section to avoid perioperative awareness and pressor response resulting from inadequate anaesthesia, analgesia, or both.

But also there is a different opinion that magnesium is not that effective in anesthesia and does not have a positive effect on neuromuscular block. Tramer and others observed that pretreatment with IV magnesium sulphate had no impact on postoperative pain and analgesic consumption, but the patients in their study received only diclofenac suppository immediately preoperatively(14). Since intraoperative magnesium is known to potentiate the analgesic efficacy of opioids, the administration of intraoperative pethidine resulted in superior pain relief in our patients. Also Ko SH et al tried to evaluate whether perioperative intravenous magnesium sulfate infusion affects postoperative pain. They say that perioperative intravenous administration of magnesium sulfate did not increase CSF magnesium concentration and had no effects on postoperative pain(15).

We administered magnesium sulphate in dosage of 50 mg/kg IV infused over 30 minutes before induction of anaesthesia without any subsequent infusion. This dosage has been reported to be safe without any adverse effects as reported by several workers(16).

Conclusion

Preoperative magnesium sulphate infusion as an adjuvant analgesic reduced postoperative pain in patients undergoing major abdominal surgery and decreases requirement of rescue analgesia. In this limited number of patients we did not find any evidence of adverse effects owing to magnesium sulphate. However, further studies should be done regarding different dosages of magnesium and comparison with established analgesic drugs and other routes of administration of magnesium sulphate.

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Case Report: Victims of the Long Term Effects of Chemical Weapons on Health in Kurdistan of Iraq

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ABSTRACT

Extensive exposure to chemical weapons such as mustard gas, nerve gas and cyanide causes high mortality, morbidity, injuries, and chronic side effects in vital organs, especially the respiratory tract.

Globally, chemical weapons have been documented as having been used since 429 BC, when they were used by the Spartans in the Peloponnesian War. In the First World War (WW1) the use of chemical agents caused an estimated 1,300,000 casualties, including 90,000 deaths. Chemical weapons were heavily used by Iraq against Iranian soldiers between1984-1986, then, against the Iraqi Kurds in Sheikh Wasan and Balisan valley, during April 1987 and in Halabja on 18th March 1988.

Reports suggested that as many as 2.9% of the Kurdish population have been exposed to chemical weapons at some level.

This case report describes a Kurdish lady who was exposed to mustard gas during a chemical attack in Sheikh Wasan in Iraq.

A forty eight years old woman wearing black clothes presented to our center at 1999 complaining from shortness of breath (SOB). Her condition started 12 years ago when the Iraqi Government attacked her village Sheikh Wasan by Chemical weapons which included Mustard gas and nerve gases such as Sarin, Tabun and VX in April 1987. She described how the gas smelled like rotten apples as it spread over the village. During the attack she suffered from sever SOB, cough, skin burn and eye irritation and lacrimation. After several days of being without medical care, she received some medical attention by local medical staff in the area because the Iraqi authorities at that time refused and prohibited them from management at the major hospitals. When she returned to her home she found that several members of her family had died during the exposure to chemical gases. Among the dead people were her parents, two brothers, husband and son, in addition to other second and third degree relatives. Since that time she has suffered from repeated attacks of cough and SOB and wheezing that were increased by exertion and cold exposure. The attacks were more severe with time and the SOB has interfered with her daily activity and eventually she was suffering from SOB at rest and during sleep that made her unable to sleep lying down. Moreover she was suffering from severe depression since that time for which she consulted several doctors but without improvement. In the end of 2001, she suffered from severe cough and Hemoptysis associated with anorexia and loss of weight. She consulted our center for this purpose and we asked for a medical care for her. Available haematological and radiological investigations were done for her showing a preliminary diagnosis of non-small cell lung cancer. . She was sent for further investigations and treatment, but since then she has been disappeared and no more information was recorded about her situation.

This is one example of many of those who suffered from the effect of chemical weapons in Kurdistan of Iraq.

Key words: Chemical weapon, Mustard gas, shortness of breath, Cancer.

Introduction

The use of chemical warfare agents dates back to 429 BC and various agents have been developed and used against populations since that time. (Table 1 - below)

The NATO definition of a chemical agent is: A chemical substance which is intended for use in military operations to kill, seriously injure or incapacitate people because of its physiological effects. (1).

- **429 B.C.** - Spartans ignite pitch and sulphur to create toxic fumes in the Peloponnesian War (CW)
- **424 B.C**. - Toxic fumes used in siege of Delium during the Peloponnesian War (CW)
- **960-1279 A.D.** - Arsenical smoke used in battle during China's Sung Dynasty (CW)
- **1346-1347** - Mongols catapult corpses contaminated with plague over the walls into Kaffa (in Crimea), forcing besieged Genoans to flee (BW)
- **1456 -** City of Belgrade defeats invading Turks by igniting rags dipped in poison to create a toxic cloud (CW)
- **1710** - Russian troops allegedly use plague-infected corpses against Swedes (BW)
- **1767** - During the French and Indian Wars, the British give blankets used to wrap British smallpox victims to hostile Indian tribes (BW)
- **April 24, 1863** - The U.S. War Department issues General Order 100, proclaiming "The use of poison in any manner, be it to poison wells, or foods, or arms, is wholly excluded from modern warfare"
- **July 29, 1899** - "Hague Convention (II) with Respect to the Laws and Customs of War on Land" is signed. The Convention declares "it is especially prohibited… To employ poison or poisoned arms"
- **1914** - French begin using tear gas in grenades and Germans retaliate with tear gas in artillery shells (CW)
- **April 22, 1915** - Germans attack the French with chlorine gas at Ypres, France. This was the first significant use of chemical warfare in WWI (CW)
- **September 25**, 1915 - First British chemical weapons attack; chlorine gas is used against Germans at the Battle of Loos (CW)
- **1916-1918** - German agents use anthrax and the equine disease glanders to infect livestock and feed for export to Allied forces. Incidents include the infection of Romanian sheep with anthrax and glanders for export to Russia, Argentinian mules with anthrax for export to Allied troops, and American horses and feed with glanders for export to France (BW)
- **February 26, 1918** - Germans launch the first projectile attack against U.S. troops with phosgene and chloropicrin shells. The first major use of gas against American forces (CW)
- **June 1918** - First U.S. use of gas in warfare (CW)
- **June 28, 1918** - The United States begins its formal chemical weapons program with the establishment of the Chemical Warfare Service (CW)
- **1919** - British use Adamsite against the Bolsheviks during the Russian Civil War (CW)
- **1922-1927** - The Spanish use chemical weapons against the Rif rebels in Spanish Morocco (CW)
- **June 17, 1925** - "Geneva Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare" is signed - not ratified by U.S. and not signed by Japan
- **1936** - Italy uses mustard gas against Ethiopians during its invasion of Abyssinia (CW)
- **1937** - Japan begins its offensive biological weapons program. Unit 731, the biological weapons research and development unit, is located in Harbin, Manchuria. Over the course of the program, at least 10,000 prisoners are killed in Japanese experiments (BW)
- **1939** - Nomonhan Incident - Japanese poison Soviet water supply with intestinal typhoid bacteria at former Mongolian border. First use of biological weapons by Japanese (BW)
- **1940** - The Japanese drop rice and wheat mixed with plague-carrying fleas over China and Manchuria (BW)
- **1942** - U.S. begins its offensive biological weapons program and chooses Camp Detrick, Frederick, Maryland as its research and development site (BW)
- **1942** - Nazis begin using Zyklon B (hydrocyanic acid) in gas chambers for the mass murder of concentration camp prisoners (CW)
- **December 1943** - A U.S. ship loaded with mustard bombs is attacked in the port of Bari, Italy by Germans; 83 U.S. troops die in poisoned waters (CW)
- **April 1945** - Germans manufacture and stockpile large amounts of tabun and sarin nerve gases but do not use them (CW)
- **May, 1945** - Only known tactical use of biological weapons by Germany. A large reservoir in Bohemia is poisoned with sewage (BW)
- **September, 1950-February, 1951** - In a test of biological weapons dispersal methods, biological simulants are sprayed over San Francisco (BW)
- **1962-1970** - U.S. uses tear gas and four types of defoliant, including Agent Orange, in Vietnam (CW)

Table 1: Chronology of biological and chemical weapons use and control, 429 B.C.–1998 (continued top of next page)

Source: (http://www.libraryindex.com/pages/1888/Proliferation-Weapons-Mass-Destruction-WMD-HISTORY-USAGE-PROLIFERATION.html")

• **1963-1967** - Egypt uses chemical weapons (phosgene, mustard) against Yemen (CW)
• **June, 1966** - The United States conducts a test of vulnerability to covert biological weapons attack by releasing a harmless biological simulant into the New York City subway system (BW)
• **November 25, 1969** - President Nixon announces unilateral dismantlement of the U.S. offensive biological weapons program (BW)
• **February 14, 1970** - President Nixon extends the dismantlement efforts to toxins, closing a loophole which might have allowed for their production (BW)
• **April 10, 1972** - "Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction" (BWC) is opened for signature
• **1975** - U.S. ratifies Geneva Protocol (1925) and BWC
• **1975-1983** - Alleged use of Yellow Rain (trichothecene mycotoxins) by Soviet-backed forces in Laos and Kampuchea. There is evidence to suggest use of T-2 toxin, but an alternative hypothesis suggests that the yellow spots labeled Yellow Rain were caused by swarms of defecating bees (CW)
• **1978** - In a case of Soviet state-sponsored assassination, Bulgarian exile Georgi Markov, living in London, is stabbed with an umbrella that injects him with a tiny pellet containing ricin (BW)
• **1979** - The U.S. government alleges Soviets use of chemical weapons in Afghanistan, including Yellow Rain (CW)
• **April 2, 1979** - Outbreak of pulmonary anthrax in Sverdlovsk, Soviet Union. In 1992, Russian president Boris Yeltsin acknowledges that the outbreak was caused by an accidental release of anthrax spores from a Soviet military microbiological facility (BW)
• **August, 1983** - Iraq begins using chemical weapons (mustard gas), in Iran-Iraq War (CW)
• **1984** - First ever use of nerve agent tabun on the battlefield, by Iraq during Iran-Iraq War (CW)
• **1985-1991** - Iraq develops an offensive biological weapons capability including anthrax, botulium toxin, and aflatoxin (BW)
• **1987-1988** - Iraq uses chemical weapons (hydrogen cyanide, mustard gas) in its Anfal Campaign against the Kurds, most notably in the Halabja Massacre of 1988 (CW)
• **September 3, 1992** - "Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction" (CWC) approved by United Nations
• **April 29, 1997** - Entry into force of CWC
• **1998** - Iraq is suspected of maintaining an active CBW program in violation of the ceasefire agreement it signed with the UN Security Council. Baghdad refuses to allow UNSCOM inspectors to visit undeclared sites (CW/BW)

Table 1: Chronology of biological and chemical weapons use and control, 429 B.C.–1998

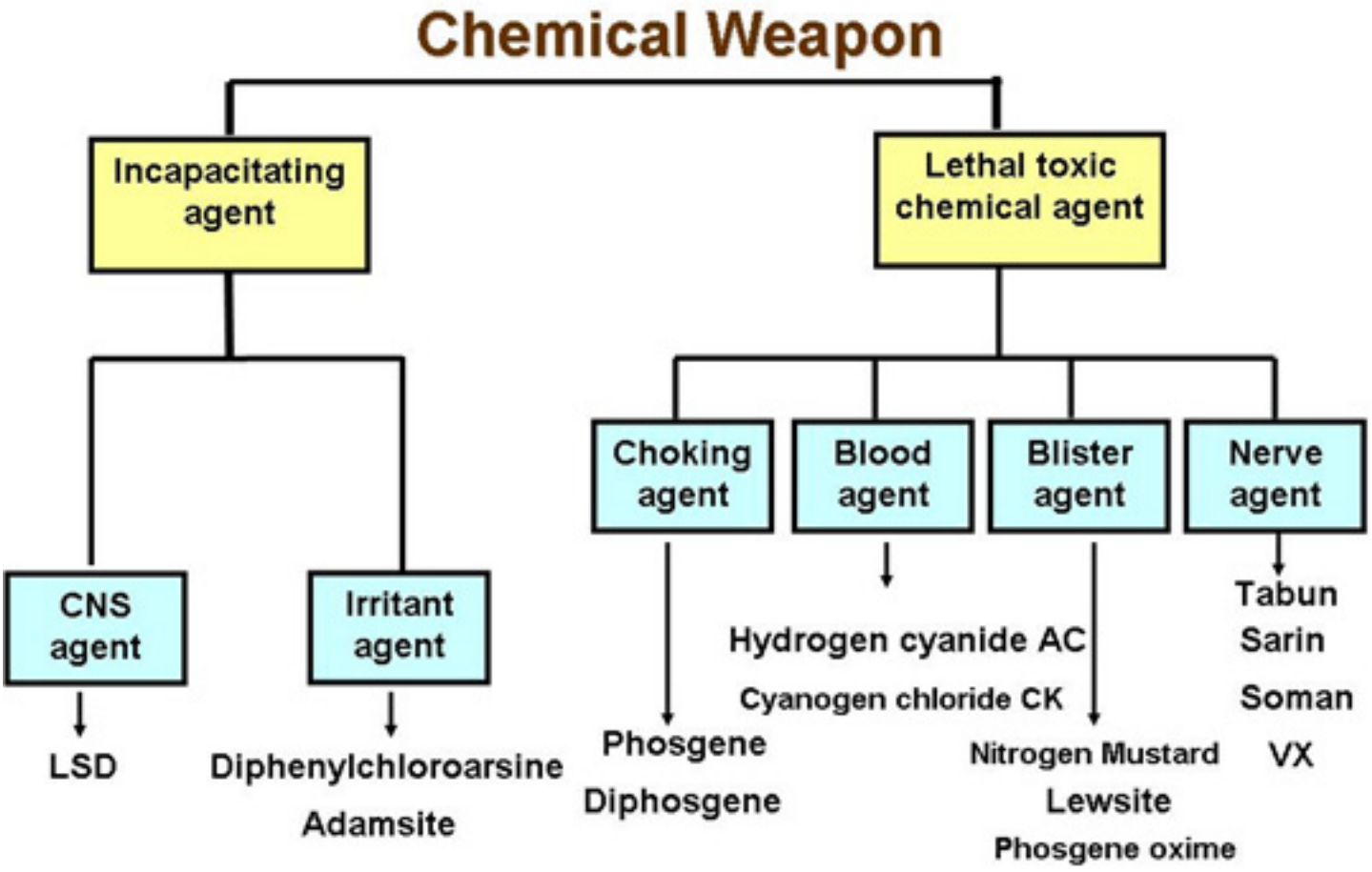

Figure 1: Classification of chemical weapon according to their mechanism of action

About 70 different chemicals have been used or stockpiled as chemical warfare agents during the 20th century and the 21st century. These agents may be in liquid, gas or solid form. Liquid agents are generally designed to evaporate quickly; such liquids are said to be volatile or have a high vapor pressure. Many chemical agents are made volatile so they can be dispersed over a large region quickly These agents were designed specifically to harm people by any route of exposure and to be effective at low doses (2).

Chemical Weapons can be divided into lethal and incapacitating categories (Figure 1).

A substance is classified as incapacitating if less than 1/100 of the lethal dose causes incapacitation, e.g., through nausea or visual problems. The limit between lethal and incapacitating substances is not absolute but refers to a statistical average. In comparison, it may be mentioned that the ratio for the nerve agents between the incapacitating and lethal dose is approximately 1/10. Chemical warfare agents are generally also classified according to their effect on the organism. The two major threat classes of chemical weapons are mustard gas and the nerve agents, and this has not changed in over 50 years. Both types are commonly called gases, but they are actually liquids that are not remarkably volatile. (3, 4).

It must also be remembered that possible new agents are constantly being discovered, and also, that some chemical agents may be used together as a mixture. From the medical standpoint, toxins could pose similar problems to those produced by chemical agents. (1)

Chemical agents in the modem sense were first used in World War I when chlorine gas was released, from large cylinders, in a favorable wind.

The French were the first to use chemical weapons during the First World War, using tear gas. The German's first use of chemical weapons were shells containing xylyl bromide that were fired at the Russians near the town of Bolimów, Poland in January 1915 (5). Official figures declare about 1,176,500 non-fatal casualties and 85,000 fatalities directly caused by chemical warfare agents during the course of the war (6).

Later in the War they used mustard gas. Soon both sides were using chemical warfare extensively leading to the introduction of gas masks. The fear of the detrimental effects of chemical warfare caused many countries to abstain from using it and except for the use of poison gas by the Italians in the war against Ethiopia (1935-36) and by the Japanese against Chinese guerrillas (1937-42), chemical warfare was not employed after World War I. This is not to say however, that the military powers of the world did not continue to develop new gases (7).

Chemical weapons were heavily used by Iraq against Iranian soldiers between1984-1986, then, against the Iraqi Kurd Table (2). In 1987-88 Iraqi forces launched chemical attacks against approximately 40 Kurdish villages and thousands of innocent civilians (8).

Initial scientific studies conducted by local doctors and international specialists indicate that as many as 2.9% of the population of almost four million people in northern Iraq have been exposed to chemical weapon at some level between April 1987 and August 1988. In April of 1987, the regime attacked the villages of Sheik Wasan and Balisan, using chemical weapons for the first time, killing more than a hundred people Figure (2), mostly women and children. The worst of these attacks devastated the city of Halabja on March 16, 1988. (9) The attack on Halabja, a town of 80,000 to 90,000 people, is the largest chemical attack against civilians in history (10).

The Halabja attack involved multiple chemical agents including mustard gas, and the nerve agents SARIN, TABUN and VX. Some sources report that cyanide was also used. It may be that an impure form of TABUN, which has a cyanide residue, released the cyanide compound. Most attempts directed to developing strategies against chemical or biological weapons have been directed towards a single threat. The attack on Halabja illustrates the importance of careful tactical planning directed towards more than one agent, and specific knowledge about the effects of each of the agents. More than 5000 people were killed during the attack on Halabja, and more than 20,000 were injured (11).

Date	Area Used	Types of agents	Approximate casualties	Target Population
Aug-83	Hajj Umran	Mustard Gas	Fewer than 100	Iranians/Kurds
Oct. - Nov 1983	Panjwin	Mustard Gas	3000	Iranians/Kurds
Apr-87	Balisan Vali	Mustard/Nerve agent	Hundreds	Kurds
Mar-88	Halabja	Mustard/Nerve agent	5000	Kurds

Table 2: Documented Iraqi Use of Chemical Weapons on the Kurds

Figure 2: Samples of chemical weapon used in Balisan Vali in 1987.

Today at Balisan and Sheikh Wassan, 23 commemorative graves are representing 233 lost in the attack. The remains of the dead were too difficult to separate and identify Figure (3).

Figure 3: Today at Balisan and Sheikh Wassan, 23 commemorative graves are representing 233 lost in the attack

Unlike Halabja, the Balisan valley is far from the Iran border Figure 4. Injured survivors seeking treatment at hospitals in government-controlled Arbil were taken away by the security forces -- and many were never seen again.

Residents of the villages recall that planes appeared, dropping canisters that spewed yellow dust. The dust was mustard gas, but most civilians did not recognize the danger until symptoms appeared hours later. Many who did not die in the attacks were permanently blinded; children and the elderly were particularly affected.

Extensive exposure to chemical weapons such as mustard gas, nerve gas and cyanide caused high mortality, morbidity, injuries, and chronic side effects in vital organs, especially the respiratory tract (12).

Mustard a poisonous chemical agent is a cell poison that causes disruption and impairment of a variety of cellular activities. Mustard is an alkylating agent, and once absorbed, its toxic effects result from chemical reactions with cellular constituents. These biochemical reactions cause inhibition of mitosis, nicotinamide adenine dinucleotide (NAD) depletion, decreased tissue respiration, and ultimately, cell death (13, 14,15).

Figure 4: Location of Balisan Vali and Halabja in northern Iraq

Mustard agent was produced for the first time in 1822 but its harmful effects were not discovered until 1860. Mustard agent was first used as a CW agent during the latter part of the First World War and caused lung and eye injuries to a very large number of soldiers. Many of them still suffered pain 30-40 years after they had been exposed, mainly as a result of injuries to the eyes and chronic respiratory disorders (16)

Mustard agents are usually classified as “blistering agents” owing to the similarity of the wounds caused by these substances resembling burns and blisters. It produces blisters and damage to skin, eyes, respiratory and gastrointestinal tracts. There is usually erythema; vesication; burns and lung damage. Mustard gas also affects many other systems including haematopoietic and immune systems. Haematological effects include leucopenia, thrombocytopenia, decrease in RBCs and sepsis. Secondary infections of damaged tissue can occur easily. The most serious of the long term effects arise because mustard gas is carcinogenic and mutagenic. In the respiratory system there are increased risks of chronic lung disease, asthma, bronchitis. Permanent impairment of vision may occur and eye damage may be severe, leading to blindness. Skin lesions and burns may be severe with persistent changes and hypersensitivity to mechanical injury. Carcinogenic and mutagenic effects can result in cancers, Carcinogenic and mutagenic effects can result in cancers, congenital malformations and infertility. Long term effects (mutagenesis, carcinogenesis, eye, skin, lung, fertility) etc are dose and route dependent (17, 18, 19).

Case report

This case report describes a Kurdish lady who was exposed to mustard gas and nerve agent during a chemical attack in Sheikh Wasan and Balisan vale in Iraq.

Figure 5: Badriya Saed Khidir

A forty eight year old woman wearing black clothes presented to our center at 1999 complaining from shortness of breath (SOB). Her condition started 12 years ago when the Iraqi Government attacked her village Sheikh Wasan by Chemical weapons which included Mustard gas and nerve gases such as Sarin, Tabun and VX in April 1987. She described how the gas smelled like rotten apples as it spread over the village.

During the attack she suffered from severe SOB, cough, skin burn and eyes irritation and lacrimation. After several days of being without medical care, she received some medical attention by local medical staff in the area because the Iraqi authorities at that time refused and prohibited them from management at the major hospitals. When she returned back to her home she found that several members of her family have died during the exposure to chemical gases. Among the dead people were her parents, two brothers, husband and son, in addition to other second and third degree relatives. Since that time she has suffered from repeated attacks of cough and SOB and wheezing that were increased by exertion and exposure to cold. The attacks were more severe with time and the SOB has interfered with her daily activity and more recently she was suffering from SOB at rest and during sleep that made her unable to sleep lying down. Moreover she was suffering from severe depression since that time for which she consulted several doctors but without improvement.

In the end of 2001, she suffered from sever cough and Hemoptysis associated with anorexia and loss of weight. She consulted our center for this purpose and we asked for medical care for her. Available haematological and radiological investigations were done for her showing a preliminary diagnosis of non-small cell lung cancer. She was sent for further investigations and treatment, but since then she had disappeared and no more information was recorded about her situation.

On the 17th of March 2009 I visited the area which were exposed to chemical weapon in 1987. In Balisan I asked about a woman called Badriya Saed Khidir and they showed me her grave saying she had passed away several weeks before. She died while her eyes were filled with tears crying for the fate of her son, her parents, her two brothers and her lovely husband.

Another victim was a baby girl. Her family named her Chemia (Chemist) because she was borne on 16th April 1987 on the day of the attack in Sheikhwasan. She died after three months from the exposure to chemical attack.

These are two examples of the many who suffered from the effect of chemical weapons in Kurdistan of Iraq.

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Figure 6: Grave of Badriya Saed Khidir

Figure 7: The author visiting the grave of Badriya Saed Khidir

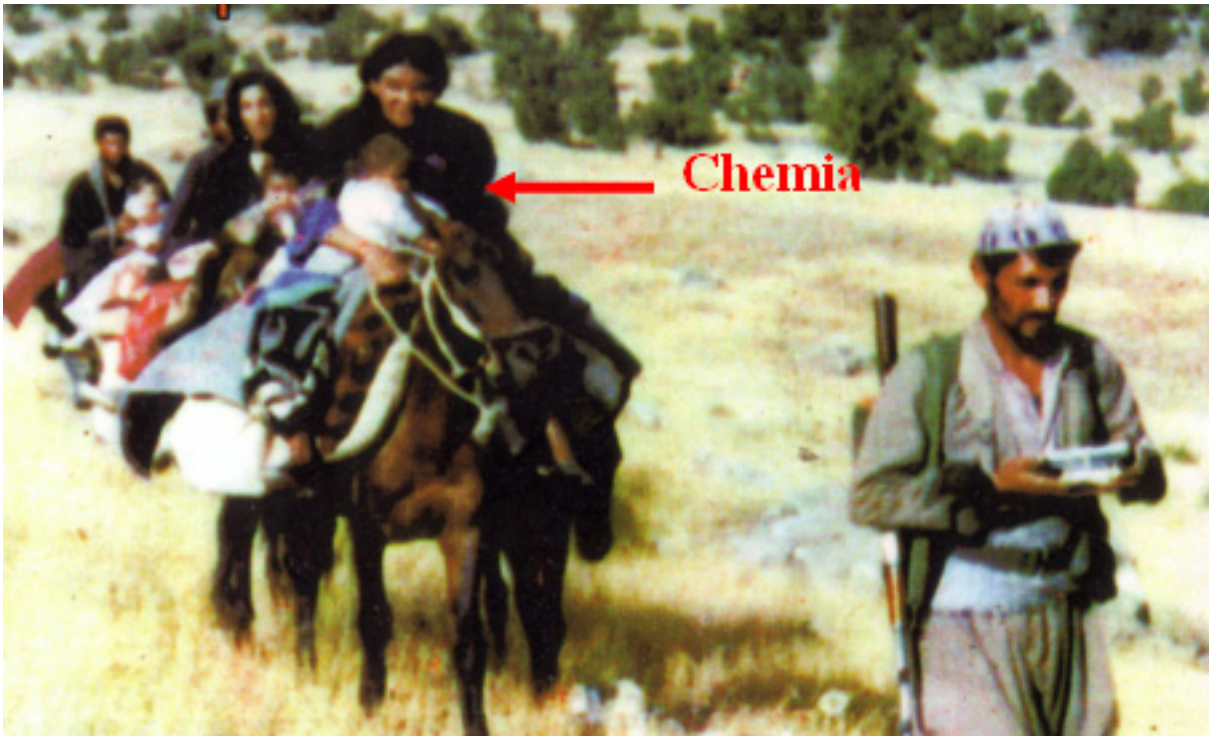

Figure 8: A family escaping from area exposed to chemical weapon in Balisan Vale

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Acardia /Acephalic Twin Monster: Lessons for the Developing Countries

ABSTRACT

We report a case of twin gestation (monochorionic diamniotic) in which one of the twins was an acardiac, acephalic. His co-twin suffered growth retardation and early neonatal death. Twin incidence in the Yoruba ethnic group is very high [6 per 100 births]; ironically this is the first report of acardiac monster in Nigeria if not in the African continent; only 8 percent of deliveries are conducted by doctors in Nigeria.

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Introduction

Most documentations of acardia/acephalic twin abnormalities were from developed nations with twin incidence less than 30 percent in Nigeria. Fetal abnormalities are sensational reports by journalists in Nigeria; many claims are not substantiated by facts. Over 63 percent of deliveries in Nigeria occur outside the health institutions with only 8 percent attended by doctors[1] giving room for sensational reports. Faith healers and spiritual homes had reported fetuses delivered with appearances of monkeys, lizards or resemblance of stones, since medical knowledge of such people are limited, this abnormality may not be rare. A search through the literature has not confirmed an earlier report of this condition in Nigeria and probably the African continent. The purpose of this report is to bring to light, lessons learnt in the diagnosis and management of such a rare fetal abnormality.

Case report

Mrs F.A, was an unbooked 29 year old gravida 3 para 2 Nigerian whose mother delivered a set of twins. She presented with abdominal pain at a gestational age of 37 completed weeks. Examination revealed a healthy young woman, not in painful distress. Symphysio fundal height was 43 centimetres, fetal parts difficult to palpate and fetal heart sound was audible. Cervical os was closed. A diagnosis of multiple gestation with polyhydramnios was made.

Ultrasonic scan - a live fetus compatible with 29 weeks of gestation with polyhydramnios coexisting with a cystic ovoid structure measuring 14.1 cm by17.3 cm.A diagnosis of a live fetus with aberrant placental with venous lakes [hydropic placenta] was made.

4 days later she had a spontaneous vaginal delivery of a severely asphyxiated female, birth weight 1 kilogramme and Apgar score of 2 in 1 minute. Head circumference 32 cm, crown heel length of 38cm. The baby died after 25 minutes of resuscitation.

Uterine contractions ceased after the delivery of the first twin.

Examination of the abdomen : symphysio fundal height was 41cm, fetal heart was not audible.

Vaginal examination revealed a cervical dilatation of 6 cm and a firm mass was palpable in the lower uterine segment, a diagnosis of intra uterine tumour with retained placenta was made.

At exploratory laparotomy, an acephalic twin in frank breech presentation was observed. She was a female weighing 1.75kilogrmme, well formed from the umbilicus to the lower limbs, dilated umbilicus with rudimentary upper section of the body with no distinct feature. Other features included polyhydramnios, placenta weight of 1.6 kilogram.

Histology of the placenta showed numerous chorionic villi covered by cytotrophoblast, syncytiotrophoblast, with syncytial knots and fetal membranes.

(See Figure 1 - next page)

Discussion

The incidence of acardia/acephalic twin abnormality is reported as 1: 34600 births [2] and represents an underestimated ratio considering geographical variation of twinning. The Yoruba ethnic group in Nigeria has the highest twin ratio in the world at 5.7 per 100 births [3]. The case presented belongs to this ethnic group and her mother had a set of twins. The incidence of twinning in our hospital is 6 per 100 births. This incidence of acardiac, acephalic twin may be more considering only 8 percent of deliveries in Nigeria are conducted by doctors with only a fraction having the opportunity to report such abnormalities even when they are able to identify such. The ratio of monozygotic twinning is about 1:250 births and that 1% of all twin births is

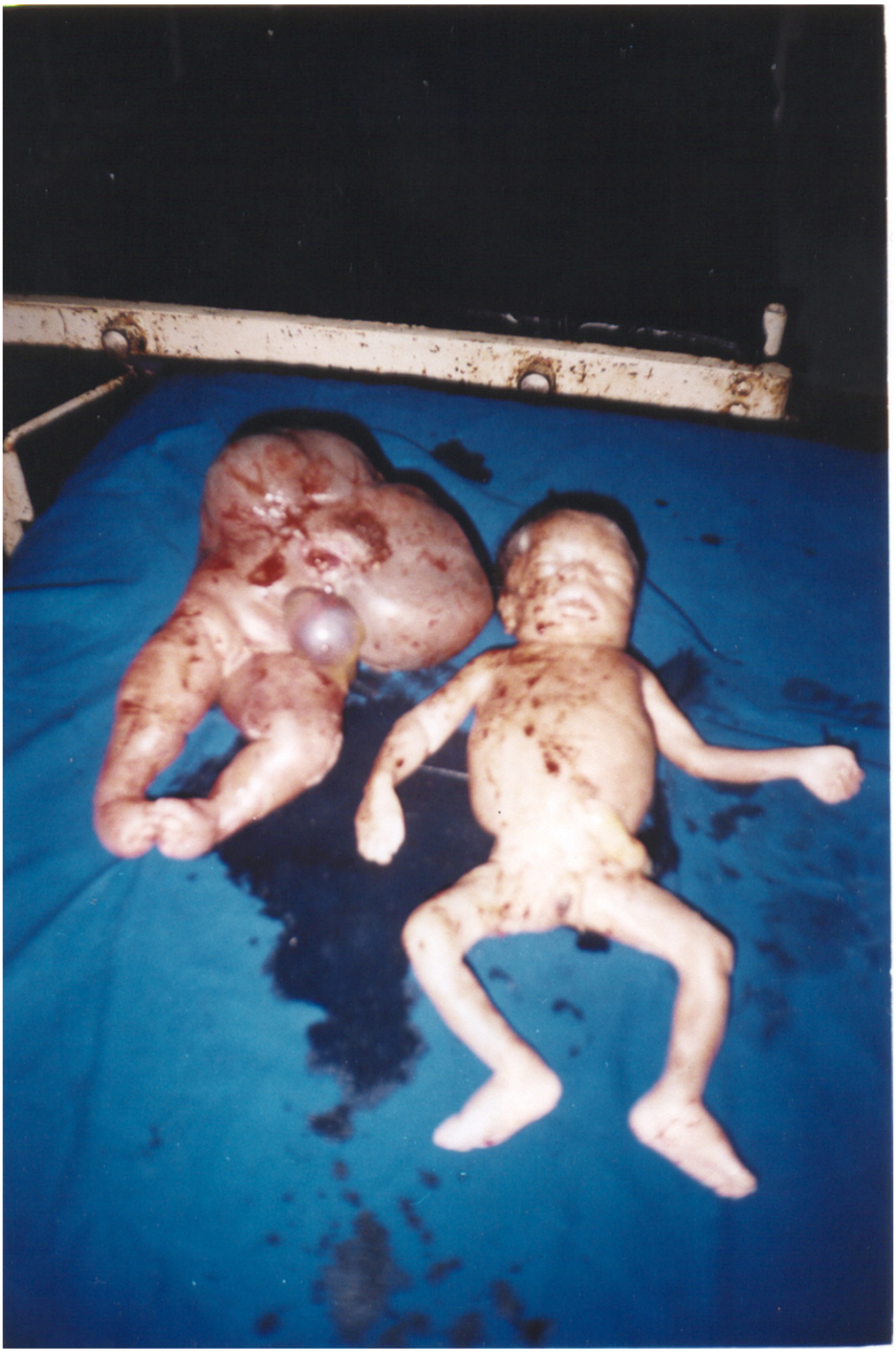

Figure 1: Acardia Acephalic Twin Monster

monoamniotic [4]. This translates to a possible higher monozygotic twinning in regions with a higher population especially regions with high twin incidences. 3.73 percent of all intra uterine death in twins occur in monochorionic gestation[5]. A lot of these abnormalities would be unrecognized in abortuses and macerated fetuses. It is interesting to know that not a single item of literature on this subject is known to have originated from Africa.

A family history of twinning was obtained and examination of the patient suggested multiple gestation but the ultrasound scan report was misleading. The pump twin was morphologically normal; fetal age of 29 completed weeks at a gestational age of 37 completed weeks could have suggested growth retardation. Polyhydramnios which is a sign of heart failure was not appreciated due to absence of overt hydrops in the pump twin. Ultrasonic features of acardia twin usually include impaired or absent development of cephalic pole, heart, upper limbs and viscera. The lower limbs are relatively well preserved, although clubbing and abnormal toes are common. The appearance is so pathognomonic that the diagnosis could be made as early as 10 weeks[6]. A two vessel cord is the rule in 66 percent of cases[7].

A well trained, experienced sonologist with a very sensitive ultrasound probe may be able to report fetal abnormality of this nature. In our practice, obsolete machines coupled with inexperience are paramount, hence the condition should be suspected in singleton gestation associated with an intra amniotic tumor [3] as suggested in this case where an ovoid cystic mass was identified by ultrasound scan but reported as aberrant placenta.

There was cessation of uterine contractions after the delivery of the first twin, and genital exploration led to the palpation of a firm mass in the lower uterine segment in a woman with undiagnosed twin gestation. Dystocia is a common complication of labour in this condition. A delay of 8 hours had been reported necessitating oxytocin use[.8] The absence of a fetal heart in a patient with symphysio fundal height compatible with 41 weeks of gestation and a palpable intra uterine mass not a fetal limb (extended breech) led to exploratory laparotomy. The caesarean operation was highly regrettable though unavoidable under our circumstance.

Mid trimester hysterotomy is a useful intervention in cases of twinning when one fetus is a threat to the health of the other [9], hence elective caesarean operation at the time of presentation would have improved perinatal outcome since the pump twin has a mortality rate of 50% as a result of high-output heart failure when conservative management is continued[10]. Therapeutic abortion is no longer indicated at prenatal diagnosis of an acardiac fetus and a healthy twin despite the risk of invasive treatment[10].

Endoscopic laser coagulation at or before 24 weeks and endoscopic or sonographic guided umbilical cord ligation after this gestational age seem to be the best treatments for this condition, but which is still not feasible in developing nations[10]. Other forms of invasive therapies include a steel coil placed in the umbilical cord close to the abdominal wall of the acardiac monster under ultrasonographic guidance at 23 weeks of gestation to block blood flow. As a result, no enlargement of the acardiac monster was observed, and the cardiac function of the unaffected fetus improved. At 38 weeks of gestation, the patient delivered a normal baby weighing 2,237g and an acardiac monster weighing 110g. There were no complications in either the mother or newborn.[11]

Recommendations: High level of surveillance for Twin Reversed Arterial Perfusion syndrome in women with complicated pregnancies where ultrasonic scan is unable to detect more than one morphologically normal fetus.

Polyhydramnios though common with uniovular twin, may be a warning sign of cardiac failure in a distress twin.

Elective caesarean section at the age of fetal viability i.e between 32-34 weeks of gestation subject to neonatal services would improve perinatal morbidity of the fetus since conservative medical management is unrealistic in our practice.

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