Seasonality, Epidemiology and Outcome of Congenital Diaphragmatic Hernia in South West of Iran

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ABSTRACT

Introduction: The pathogenesis of congenital diaphragmatic hernia (CDH) is not clear. Risk factors including environmental factors have been implicated in the pathogenesis of few congenital anomalies. We aimed to assess the effect of season on the incidence of CDH and mortality rate in the southwest of Iran.

Material and Methods: In this retrospective study, the records of 60 patients with CDH who were admitted at Neonatal Intensive Care Unit (NICU) of Imam Khomeini Hospital of Ahvaz, Iran were evaluated.

Results: Assuming that all the neonates born with CDH in the region reach this hospital, overall CDH prevalence rate was 1.09 per 10,000 total births. Conceptions in spring and summer in this region had statistically significantly higher incidence of CDH. Survival rate in the series was 41.6%.

Conclusion: Seasonal variation has impact on the incidence of CDH. Mortality rate in neonates with CDH is still very high.

Key words: Congenital Diaphragmatic Hernia; Risk Factors; Seasonal variations

INTRODUCTION

Congenital Diaphragmatic Hernia (CDH) is a malformation of the diaphragm, that secondary to persistence of a defect in the diaphragm, the abdominal contents protrude into the thoracic cavity [1]. Development of the diaphragm starts during the 4th week of gestation and completed by 8th weeks. But in the fetuses with CDH, the diaphragm doesn’t close completely during this period [2]. The prevalence of CDH is reported to be from 2.4 to 4.9 per 10000 births [3,4]. The pathogenesis and etiology of CDH is complex and remains poorly understood. Nitrofen and retinoids has been known to induce CDH in animal models [5-9]. Prenatal exposure to various maternal factors such as alcohol, smoking, peri-conceptional low intake of retinol, obesity and antimicrobial drugs have been also indicted [1,10,11]. Genetics also probably plays a role [12].

McKeown and Record in 1951 performed one of the earliest analysis of the seasonal pattern in the prevalence of congenital malformation and found that more cases of anencephaly were born in the autumn and winter [13]. Many perinatal risk factors for the development of congenital malformation may be seasonal such as air pollution, influenza virus, other infectious agents, dietary intake, and pesticides [14].

The survival rate for CDH in the United Kingdom was reported to be 64.6% at 1 week, 58.4% at 1 year and 57.1% at 20 years [15].
The aims of this study are to assess the effect of season on the incidence and epidemiology and outcome of CDH in the southwest of Iran.

**MATERIALS AND METHODS**

Imam Khomeini Hospital of Ahvaz is the only referral center in the Khuzestan province of Iran having neonatal intensive care unit (NICUs) and pediatric surgical services. We did a retrospective outcome analysis of the neonates presenting to us with CDH over a 5-year period (March 2011 to February 2016). Maternal factors (age, the route of delivery, month of conception) and neonatal demographic characteristics (sex, gestational age, birth body weight) were recorded. The laterality of CDH was noted. Time of onset of respiratory distress, beginning of intubation and of mechanical ventilation, date of operation (days after birth) were also noted. Nitric oxide, high frequency oscillatory ventilation (HFVO) and Extra-corpooreal Membrane Oxygenation (ECMO) were not available in our center; the neonates complicated with pulmonary hypertension were treated with hyperventilation, milrinone or magnesium sulfate.

Statistical analysis

Descriptive analysis was performed. Data are reported as frequencies, means and standard deviation. Associations of selected variables with the outcomes were assessed with chi-squared tests, logistic regression models and proportional odds models.

**RESULTS**

Of the 548052 live births over the 5-year-period in the Khuzestan province, 60 neonates with confirmed diagnosis of CDH were admitted at NICU of Imam Khomeini Hospital of Ahvaz. With an assumption that no CDH was missed, it gives an overall CDH prevalence rate of 1 per 10000 total births. There was slightly higher incidence noted for males; M: F ratio being 7:5 (Table 1). Mean birth weight was 2944.17±75 gm, (range 1100-4100). Majority of the CDH were left-sided with only 4 being right-sided; it was bilateral in one neonate.

This study shows the effect of seasonal variation on the prevalence of congenital diaphragmatic hernia in Khuzestan (Tables 2, 3).

Nine (26.4%) of patients succumbed after surgery (Table 4). The patients that survived were hospitalized for 17.96±2.13 days (range 8-55 days). Finally, 25 (41.6%) of patients discharge alive from hospital. However, the patients were not followed after discharge from the hospital.

**DISCUSSION**

Conceptions in spring and summer were known to be significantly associated with increased prevalence of CDH in this study. The effect of season on the
prevalence of CDH has been reported earlier too [16]. CDH is known to occur more frequently after maternal influenza/fever during the first trimester [14]. Seasonal peaks (January) corresponding with influenza season was detected for CDH, but this association did not reach statistical significance [17]. However, other studies did not find any association between seasonal variation and prevalence of diaphragmatic hernia [18-20].

This study showed that survival significantly affected by delivery route. There are several reports that elective cesarean section is associated with persistent pulmonary hypertension [26, 27]. No statistically significant associations were found in any maternal age categories, which is compatible with the previous study [3]. Survival in term babies was significantly higher than in preterm babies; this fact is universally acknowledged [28]. Early presentation of respiratory distress significantly affected the survival of patients that may be a reflection of the severity of lung hypoplasia or pulmonary hypertension. The side of herniation did not affect the survival of our patients; this is in contrast with an earlier study by Grizelj et al [29]. Survival rate of 41.6% in our series is lesser than survival rate among neonate with that reported from Croatia, France, England, America -47.9%, 47%, 69% and 81% at discharge respectively [28-31]. Higher mortality rate in our center probably results from inaccessibility to nitric oxide, HFO, and ECMO.

### CONCLUSION

The incidence of CDH in the southwest of Iran is 1.09 per 10 000 total births, which is so less than reported prevalence of other countries. Also conceptions in spring and summer were significantly associated with increased prevalence of congenital diaphragmatic hernia. Mortality of newborns with congenital diaphragmatic hernia in the southwest of Iran is higher than reported studies of other countries with modern technology.

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Ahvaz has the world’s worst air pollution according to a survey by the World Health Organization in 2011 [21]. This situation is exaggerated by drought and reduced rainfall and soil moisture during spring and specially summer. One of the major origins of this air pollution is Iraq. It has been suggested that war-created pollution is a major cause for increasing the prevalence of birth defects in Iraq [22].

In this study, the prevalence of CDH was 1.09 per 10000 live born infants; this is far lower than other studies. In a study including only live birth neonates prevalence of CDH were reported 2.38 per 10000 [23]. Another study that includes live births, stillbirths, miscarriages, termination of pregnancy. The prevalence of CDH in another study that includes live births, stillbirths, miscarriages, termination of pregnancy was reported 4.90 per 10000 [4]. The probable reason for the low prevalence of CDH in our study could be that we don’t receive all the neonates; the sicker ones die before they are referred to our facility. The sex ratios calculated in this study are comparable to the highest ratios previously reported in the literature [24, 25].
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