

# Risk Factors for Transient Tachypnea of New Born

Raad Fathi Abdulla<sup>1</sup>, Ali Mohammed Ayoub<sup>2</sup>, Ghazwa Mohammed Ibrahim<sup>3</sup>

<sup>1,2,3</sup>M. B. Ch. B. DCH., Al- Salam Teaching Hospital, Iraq

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## ABSTRACT

This prospective study was carried out on one hundred New born babies with birth weight of 3000 gm to 4200gm and whose mother ages between 20 years to 34 years and gestational ages range from 37-42weeks, were admitted to neonatal unit in obstetric and gynecologica teaching hospital in Al- Sulimani city, with transient tachypnea of new born during the period of (6) months from 1st June 2010 to 30th November 2010. In this study the pathophysiology, risk factor, clinical presentation. Chest x-ray finding. Another one hundred new borne with birth weight and maternal age and gestational age meaning matched with the cases of transient tachypnea who were seen in the same neonatal care unit, in the same period with problems, other than transient tachypnea were taken as a control group and risk factors were compared between them. It was found that 64 patients (64%) were males and 36 patients (36%) were females, that mean about two third are males and third are females. Sixty-One patient (61%) were delivered by cesarean and 39 patients (39%) were delivered by normal vaginal delivery. Also it was found that 68 patients (68%) their gestational ages were between 37-39 weeks and 32 patients (32%) with gestational ages between 40-42weeks. Thirteen patients (13%) from asthmatic mothers and 11 patients (11%) from diabetics' mothers and 4 patients (4%) admitted from twin delivery. Sixty-three patients (63%) their birth weight was ranging from 3000-3400 gm and 37 patients (37%) their birth weights were ranging from >3400-4200 gm. Chest x-ray show prominent central vascular marking, fluid in the lung fissures, over aeration and flat diaphragm, occasionally a small pleural effusion with no air Broncho grams and reticule-granular pattern.

**Key word:** risk factors, transient tachypnea, new born

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## INTRODUCTION

Transient tachypnea of the new born is a self-limited condition. Characterized by tachypnea shortly after birth with respiratory rate more than 60 beat/mint, mild retraction, nasal flaring and occasional expiratory grunting, usually without signs of severe respiratory distress<sup>(1,2)</sup>

Patient usually recover rapidly within 3 days. TTN is the most common cause of neonatal respiratory distress constituting more than 40% of cases<sup>(4,5)</sup>

### Etiology

During fetal life the lungs make a special fluid that fills the lungs and helps them to grow. Fetal lung fluid is essential for normal lung development, the fluid within the fetal lung arises from the lung and does not merely represent aspirated amniotic fluid. When the volume of fetal lung fluid is abnormally small, lung hypoplasia occurs, as in conditions such as oligohydramnios<sup>(6)</sup> In contrast excess fetal lung fluid result in lung over growth (hyper plasia)<sup>(7)</sup> Fetal lung fluid secretion arises from active Cl-secretion by the fetal distal lung epithelia<sup>(8,9)</sup>

### Patho physiology

During the fetal life the lungs are expanded with an ultra filtrate of the fetal serum in the course of neonatal transition, this ultra filtrate must be removed and replaced with air. The classic explanation for how this occurs was that passage through the birth canal would by squeezing the thorax, help eliminate the liquid in the lungs<sup>(14)</sup> With the remaining fluid being removed by pulmonary capillaries and the lymphatic:<sup>(1,13,14)</sup>

Currently, however the bulk of this clearance is thought to be mediated by trans epithelial sodium re absorption through sodium channels in the alveolar epithelial cells.

Only a limited contribution from mechanical factors and starling forces. Hormonal changes of the fetus and mother, brought about mainly by the onset of spontaneous labor, prepare the fetus for the neonatal transition to air breathing<sup>(14)</sup> TTN occurs when the liquid in the lung is removed slowly or incompletely; correlate with a decreased thoracic birth squeeze or diminished respiratory effort in the new born<sup>(15)</sup>.

### Cellular mechanism that Result in Epithelial $\text{Na}^+$ Transport.

Active ion transport play a critical role in the liquid movement across the fetal and perinatal lung epithelium<sup>(15)</sup> To transport  $\text{Na}^+$  actively, the epithelia must possess intra cellular tight junction and be polarized.

The phenomenon where by some membrane protein are localized at the apical membrane and others are localized at the basolateral membrane<sup>(16)</sup>

Basolaterally located ATPase extrudes  $\text{Na}^+$  In exchange for  $\text{K}^+$  (3  $\text{Na}^+$  ions for 2  $\text{K}^+$  ions) and generates an approximate 10- fold chemical gradient between the intra cellular and extra cellular fluid.

This action, combined with basolateral  $\text{K}^+$  channels, which create an intra cellular electrical potential of approximately - 40 mV.

The  $\text{Na}^+$  electrochemical gradient "drags  $\text{Na}^+$ " into the cell a long with  $\text{Cl}^-$  and  $\text{K}^+$  across the basolateral membrane via a  $\text{Na}/\text{K}/2\text{Cl}^-$  CO transporter.<sup>(16,17)</sup>

The negatively charged  $\text{Cl}^-$  "finds itself" within the cell that has a negative intra cellular potential, and this electrical force enables  $\text{Cl}^-$  to be "pushed upstream" against its concentration gradient out of the apical anion -selective channels.  $\text{Na}^+$  follows  $\text{Cl}^-$  through Para cellular pathways, with water flowing between or through cells via aquaporins. (Figure1).<sup>(1)</sup>

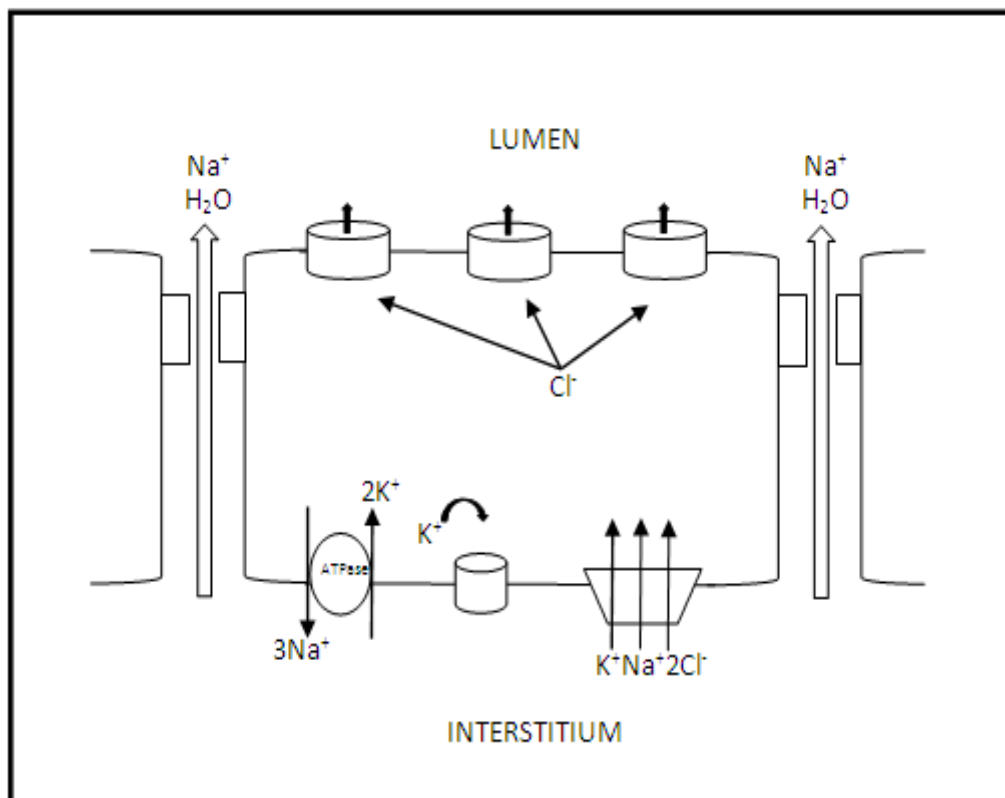
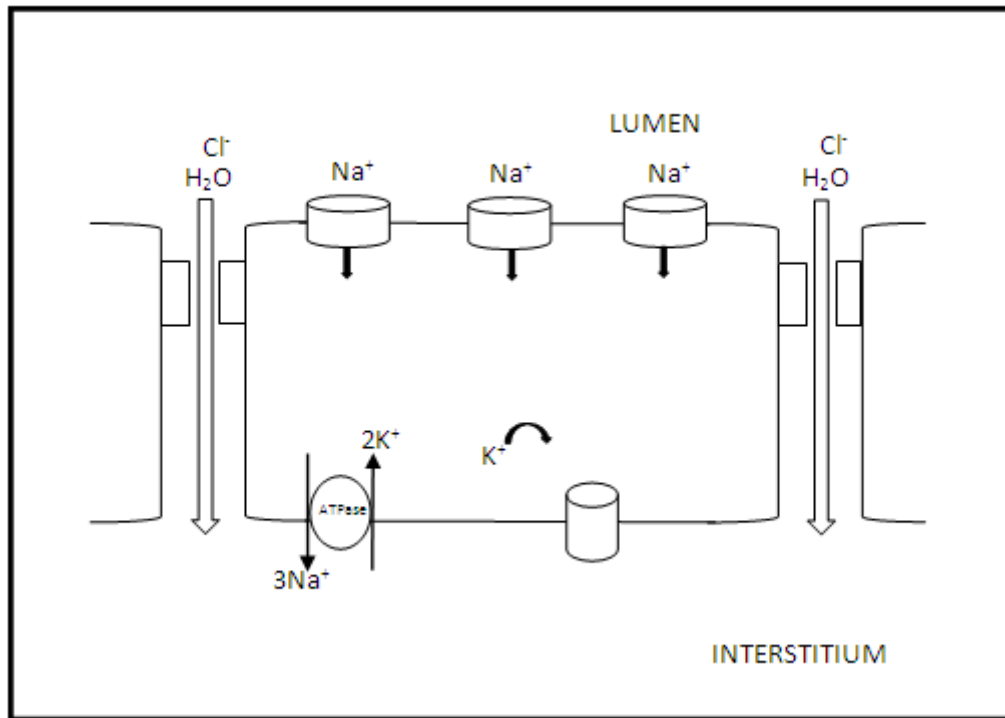


Figure 1. Model of fetal lung fluid secretion by epithelial cells

The resultant electrochemically increased gradient leads to passive  $\text{Na}^+$  absorption via apical  $\text{Na}^+$  per meant channels that is extruded by  $\text{Na}/\text{K}^+/\text{ATPase}$  out of the cell.

$\text{Cl}^-$  and water passively follow the  $\text{Na}^+$  ions although Para cellular or intracellular pathways. (Figure2).(10)



**Figure 2: Model of fetal lung fluid absorption by epithelial cell.**

An amiloride-sensitive epithelial  $\text{Na}^+$  channel (E Na c) play an important role in lung epithelial  $\text{Na}^+$  transport . And its composed of 2 alpha , one beta for lung epithelial , and one gamma sub unit.<sup>(18)</sup> Risk Factors for the development of TTN

The main risk factors for the development of TTN are :<sup>(25)</sup>

1. Mode of delivery. (elective CS)
2. Maternal diseases<sup>(5)</sup>
  - a) maternal diabetic.(macrosomia)
  - b) maternal asthma.
3. Gestational age
4. Birth weight
5. Male sex (26)
6. Multiple pregnancy

The less common risk factors <sup>(7)</sup>

- 1) Delayed cord clamping.
- 2) Rapid vaginal delivery.
- 3) Excess maternal fluid administration.

### Mode of delivery

Neonate born by elective cesarean section are frequently admitted to advanced care nurseries than neonate born to mothers intending to deliver vaginally , with an increased risk of respiratory morbidity, and the transient tachypnea of the new born was more common with CS delivery<sup>(29,30)</sup> .

During spontaneous labor there is decrease in secretion of fetal lung liquid and an increase in its absorption, and release of surfactant is stimulated, this may be mediated by raised level of catecholamine and steroid in the fetus in response to rupture of membrane and stress of labor<sup>(33)</sup> .

### Maternal Asthma

Infants of asthmatic mothers are more likely than other to have TTN, stratified analysis by sex also revealed a sex difference in the strength of the association between maternal asthma and TIN<sup>(35)</sup> . A potential proposed mechanism for this association that both mothers and infant of asthmatic mothers have a genetic predisposition to B - adrenergic hypo responsiveness<sup>(36)</sup> .

### Diabetic Mother and Twin

Although peri natal mortality among gestational diabetes and pre existing insulin dependant diabetes mellitus has been declined, excess neonatal morbidity remain a significant challenge<sup>(39)</sup>.

Macrosomia and respiratory morbidity are common sequels of diabetes.

TTN account about 16% of respiratory morbidity in diabetic mother, macrosomia remain an important morbidity because its association with increase risk for traumatic birth injury, obesity and diabetes in later life<sup>(39)</sup>.

### Clinical features of TTN

TTN its self limited condition<sup>(12)</sup> usually appear soon or within 6 hours after birth<sup>(13)</sup>, characterized by early onset tachypnea (more than 60 breath per minutes) with mild retraction and occasionally expiratory grunting and cyanosis [skin has bluish tinge around the mouth and nose], usually cyanosis require no more than 40% oxygen<sup>(13)</sup>. The symptoms can last from few hours to 3 days The lungs usually are affected diffusely and symmetrically<sup>(3,5)</sup>. The condition is commonly accompanied by a small pleural effusion and it may be difficult to distinguish TTN from other causes of respiratory distress of the new born<sup>(13)</sup>.

### Diagnosis

The mother and labor history are important to make the diagnosis, TTN usually diagnosed after monitoring your baby for 1-2 days, that mean timing is a key diagnostic factor<sup>(13)</sup> Test include.

- complete blood count with differential to look for signs of infection, such as pneumonia.
- blood culture to look for sign of infection.
- arterial blood gas determination to check the oxygen level in the babies blood.
- blood glucose monitoring hypoglycemia can cause or aggravate tachypnea<sup>(5)</sup>

### 2. Chest X-ray:

The finding on chest radiography may include mild, symmetrical lung over aeration and streaky bilateral pulmonary interstitial opacities, prominent perihilar interstitial marking and may show diffuse parenchyma infiltrates a "wet silhouette" around the heart, or intra lobar fluid accumulation and fluid in the fissures<sup>(45)</sup> occasionally there is small pleural effusion, the right side may appear more opacified than the left<sup>(13)</sup>.

### 3. Pulse Oximetry Monitoring:

A piece of tape containing an oxygen sensor is placed on babies foot, hands, its connected to a monitor that show O<sub>2</sub>%.

### Differential Diagnosis

Differentiation from other causes of neonatal respiratory distress may take time, initial evaluation, monitoring and basic supportive care must cover all diagnostic contingencies.

Following immediate postnatal culture, a course of antibiotic therapy may be initiated and then terminated at 72 hours if culture are Negative and the clinical condition improving<sup>(13)</sup>.

The condition most commonly confused with TTN are respiratory distress syndrome and group B streptococcal pneumonia.

Meconium aspiration syndrome bacterial infections take time to develop, with respiratory consequences occurring hours to days after birth, usually with risk factors include prolonged rupture membrane,<sup>(49)</sup>

Less Common Differential Diagnosis According Incidence Include<sup>(5,13)</sup>

1. Congenital heart disease
2. Congenital lymphangiectasia
3. Polycythemia
4. Cerebral hyperventilation
5. Anemia
6. Hypovolemia
7. Neurological and metabolic
8. Medication include anesthesia, analgesic
9. Persistent pulmonary hypertension of the newborn.

### Mortality and Morbidity

The TTN entail no mortality or morbidity, however it prolong the neonate hospital stay and is associated with an increase risk of asthma development during childhood<sup>(13)</sup>.

## Prognosis

TTN usually resolves completely within first 48-72 hours after delivery, babies who have had TTN usually have no further problem from it and require no special care or follow up other than their routine pediatrician visit<sup>(6)</sup>.

## Treatment

Supportive care and close monitoring are the main important points in treatment:

### 1. Oxygen (O<sub>2</sub>)

Infants may be given O<sub>2</sub> as needed to maintain an adequate blood O<sub>2</sub> level. O<sub>2</sub> requirement will usually be highest with in few hours<sup>(53)</sup>.

### 2. Supplemental Feeding:

Very rapid breathing can cause the baby to feed ineffectively, fluid may be given through vein until infants improve<sup>(53)</sup>.

### 3. Intra Venous Antibiotics

Medication is continued until the result of the blood test confirm that there is no infection, this usually take 48 to 72 hours<sup>(7,48)</sup>.

## AIMS OF THE STUDY

To study the risk factors associated with TTN, and to describe the clinical characteristics of infant with TTN in respect to the symptoms, signs and severity.

## PATIENTS AND METHODS

This a prospective study was done in neonatal intensive care unit in obstetric and gynecology teaching hospital, in sulaimani city, during the period of (6) months from 1<sup>st</sup> June 2010 to 30<sup>th</sup> November 2010.

One hundred neonate with birth weight ranging from 3000 gm to 4200 gm and whose maternal age were between 20 & 34 years, and whose gestational age ranged from 37 weeks completed to 42 weeks, with the attack of TTN were included and other one hundred neonates (birth weight, gestational age and maternal age) were matched, with no tachypnea who were seen in the same neonatal care unit taken as a control healthy group.

Diagnosis of TTN was based on respiratory rate and CXR some time showing prominent pulmonary vascular marking. To determine the risk factors associated with TTN score for each of the following risk factors: were put mode of the delivery, maternal asthma, maternal diabetic, gestational age, birth weight, maternal age, sex and multiple pregnancy (twin).

The following points were included in the history and examination of each patient with TTN: Maternal age, Gestational age (calculated on the basis of chronological criteria), Mode of delivery, Sex, Maternal disease (asthma and diabetics), Single tone or twin, birth weight. Also CXR finding, duration of hospitalization and out come. The same points were considered for the control groups.

Chest X-ray supplied with reports were performed to all studied patients at birth and after 72 hours.

## Statistical Analysis

The data were analyzed using number and percentage for description. Then Chi-square was used to find the relationship between the disease and the risk factor. For the comparison of radiological and clinical findings between the two groups, Z-test between two proportions was used. All tests were considered significant at p-value of 0.05 or less. Odd ratio was used to measure the risk of the factors on TTN occurrence in infants. It may be considered as the ratio of the odds of exposure to non-exposure among the disease (a/c) compared to the non-diseased (b/d).

## RESULTS

**Table1: Distribution of TTN patients and controls according to sex.**

Sex	TTN (n=100)		Control (n=100)		OR	95 % C.I	P-value
	No	%	No	%			
Male	64	64.0	39	39.0	2.78	1.57-4.93	0.004
Female	36	36.0	61	61			
Total	100	100	100	100			

Table (1) shows that the sex distribution was 64 patients (64%) males, about two third and 36 patients (36%) females, males to females ratio was 1.77:1, in control groups the males to females ratio was 0.64:1. The odd ratio was 2.78 with significant P value 0.004. The male sex of infant represents a risk to develop TTN by 2.78 times that of female with significance. The 95% confidence interval shows that all the values that odd ratio could catch indicate the male sex risky as in (Table1)

**Table 2: Distribution of TTN patients and controls according to the mode of delivery**

Mode of delivery	TTN (n=100)		Control (n=100)		OR	95 % C.I	P-value
	No.	%	No.	%			
C/S	61	61.0	42	42.0	2.16	1.23-3.80	0.007
Normal	39	39.0	58	58.0			
Total	100	100	100	100			

(Table2) shows that 61 patients (61%) of the newborn affected by TTN were delivered by elective CS and 39 patients (39%) of TTN normally vaginally delivered. CS to normal vaginal delivery ratio was 1.56:1, while in control group the ratio was 0.73:1.

The OR was 2.16, there is significant relationship between TTN occurrence and mode of delivery. Infants delivered by cesarian section mode were more susceptible to exhibit TTN 2.16 times those of normal mode of delivery.

In addition, the lower and upper limits of 95% confidence interval were considered risky as they were more than one as in (Table2)

**Table 3: Distribution of TTN patients and controls according to gestational age**

Gestation age (week)	TTN (n=100)		Control (n=100)		OR	95 % C.I	P-value
	No.	%	No.	%			
37-39	68	68.0	57	57.0	1.60	0.90-2.86	0.109 (NS)
40-42	32	32.0	43	43.0			
Total	100	100	100	100			

NS = Not significant

The gestational age of those with TTN from 37-39 weeks was 68% (about two third), with 57 patients (57%) in control group (about half), were TTN newborn from 40-42 weeks was 32 patients (32%), with 43 patients (43%) in control group, the ratio between (37-39) groups to (40-42) groups was 2.1:1 in TTN group and 1.33:1 in control group, and with OR of 1.6, with p value 0.109 (Table 3). There is a non-significant relationship between gestational age and TTN occurrence, although 37-39 week gestational age represented a risk for TTN occurrence by 1.6 times as in table (3).

**Table 4: Distribution of TTN patients and controls according to birth weight**

Birth Weight	TTN (n=100)		Control (n=100)		OR	95 % C.I	P-value
	No.	%	No.	%			
≥ 3000gm-3400gm	63	63.0	53	53.0	0.938	0.44- 2.03	0.87 (NS)
≥ 3400gm-3800gm	18	18.0	32	32.0	0.444	0.18-1.08	0.073 (NS)
≥ 3800gm-4200gm	19	19.0	15	15.1	1	-	-
Total	100	100	100	100			

NS = Not significant

(Table 4) shows that 63 patients (63%) of patients with TTN have had birth weight between (3000-3400 gm), only 53 patients (53%) in control group, and 18% of patients with TTN have had birth weight ranging from (>3400-3800gm), and 32 patients (32%) in control group, 19 patients (19%) of patient by TTN have birth weight between (>3800-4200gm), in contrast, 15 patients (15%) in control group. with OR of 0.938 in those patient there is weight between 3-3.4kg and p value 0.87 and OR of 0.444 with p value 0.073 in those birth weight between (>3400-3800 gm). There is a nonsignificant relationship between TTN occurrence and birth weight. No risk was recorded for the infant of 3000-4000 gm weight (OR = 0.938).

**Table 5: Distribution of TTN patients and controls according to family history of asthma**

Asthmatic Mothers	TTN (n=100)		Control (n=100)		OR	95% C.I	p-value
	No.	%	No.	1 %			
+ve	13	13.0	4	4.0	3.586	1.13-11.41	0.023
-ve	87	87.0	96	96.0			
Total	100	100	100	100			

(Table 5) shows that 13 patients (13%) of newborns with TTN were from asthmatic mothers, and only 4 baby (4%) from asthmatic mothers in control groups, with OR of 3.586 and significant P-value 0.023.

There is a significant relationship between the occurrence of TTN in infants and family history of asthma. Infants with positive family history have more than 3.5 times susceptibility to develop TTN than those with negative family history as in (Table 5).

**Table 6: Distribution of TTN patients and controls according to family history of diabetes.**

Diabetic Mothers	TTN (n=100)		Control (n=100)		OR	95% C.I	p-value
	No	%	No	1 %			
+Ve	15	15%	6	6.0	2.765	1.06-7.45	0.038
-Ve	85	85.0	94	94.0			
Total	100	100	100	100			

Table (6) shows that 15 patients (15%) of newborn with TTN were from diabetic mothers comparing to 6 patients (6%) in control group with OR (2.765).

**Table 7: Distribution of TTN patients and controls according to twin.**

Twin	TTN (n=100)		Control (n=100)		OR	95% C.I	p-value
	No.	%	No.	1 %			
Yes	4	4.0	6	6.0	0.653	0.18-2.39	0.518 (NS)
No	96	96.0	94	94.0			
Total	100	100	100	100			

NS = Not significant

Table (7) shows that only 4 patients (4%) of newborn with TTN were from twin delivery compared to 6 patients (6%) in control group with no significant P value 0.518 and OR of 0.653.

**Table 8: Distribution of TTN patients and controls according to maternal age.**

Maternal Age (year)	TTN (n=100)		Control (n=100)		OR	95% C.I	p-value
	No.	%	No.	%			
20-24	37	37.0	31	31%	1.27	0.645 2.483	0.494 (NS)
25-29	30	30.0	34	34 %	0.93 6	0.472 1.854	0.850 (NS)
30-34	33	33.0	35	35 %	1	-	-
Total	100	100	100	100			

NS = Not significant

There is 37 mothers (37%) whose age were between 20 years to 24years compare with 31mother 31n control group, with of 1.27 and p value 0.494 and 30% of patient with TTN whose maternal age between 25-29 years and in control group 34% with OR of 0.936 and p value 0.85 and 33% between 30-34 years (Table 8).

There is no significant relationship between TTN occurrence and maternal age (table 8). Odd ratios were near the neutral value of 1 with no risk or protective effect.

**Table 9: Radiological finding in infant with TTN**

Radiological finding	Birth - 3day (n=100)		Age > 3day (n=100)		p-value
	No.	%	No.	%	
Over age ration (flat diaphragm)	69	69.0	13	13.0	< 0.001
Central vascular making (streaky interstitial opacity)	63	63.0	10	10.0	< 0.001
Diffuse parenchymal infiltrate	10	10.0	0	0.0	< 0.001
Fluid in the fissures	20	20.0	0	0.0	< 0.001
Small pleural effusion	1	1.0	0	0.0	> 0.05 (NS)

NS = Not significant

Table (9) shows that over aeration (flat diaphragm) was found in 69 patients (69%) of those below 3days, and in 13 patients (13%) above 3days, central vascular marking was found in 63 patients (63%) in younger than 3days, and in only 10 patients (10%) in above 3days. Fluid in fissures (streak opacity) was found in 20 patients (20%) of those below 3days, never found after 3days, diffuse parenchyma infiltrate was found in 10 patients (10%) only before 3days age, 1% only have had small pleural effusion in < 3 days old.

There is a significant difference in all the measured radiological findings of the infants at 3day-birth and at more than 3 day age except for small pleural effusion as in table (9).

**Table 10: Clinical finding in infant with TTN according to less and more than 3 day age**

Clinical features	From birth 3 day		> 3day		p-value
	No.	%	No.	%	
Tachypnea	100	100.0	18	18.0	2 < 0.001
Chest retraction	64	164.0	5	5.0	< 0.001
Expiratory grunting	34	34.0	2	2.0	< 0.001
Cyanosis	21	21.0	0	0.0	< 0.001

Table (10) shows that the clinical features tachypnea was found in all patients, only 18 patients (18%) tachypnea persists after 72 hours, 11 patients of them were males. Chest retraction was found in 64 patients (64%) below 72hours, expiratory grunting was found in 34 patients (34%) below 72 hours, less, cyanosis present in 21 before 72hours age 14 patients males and 7 patients females, with no more cyanosis after this ages. There is a significant difference in the clinical features between TTN infants at 3 day birth and at more than 3 days of age ( $p < 0.001$ ) as in table (10).

## DISCUSSION

The age ranging of infant with TTN was zero to 6 hours after birth, the mean age was 1 hour plus minus 30 minutes. This is in agreement with Asenjo M. (2007)<sup>(13)</sup> had found TTN appears soon after birth, and Lewis R A.(2006)<sup>(6)</sup> TTN usually seen shortly after delivery.

The sex distribution was 64% males (about two third), 36% females (about one third), male to female ratio was 1.77:1. The OR was 2.78 that means males affected 2-3 folds more than females, with significant P value., This is in agreement with Dani C. et al (1999)<sup>(25)</sup>, and Asenjo M (2007)<sup>(13)</sup> had found TTN occur more frequently in males, with significant association between sex and TTN. Sixty one of the newborn affected by TTN were delivered by elective CS and 39% of TTN were delivered by normal vaginal delivery. CS newborn TTN to vaginal delivery ratio was 1.56:1.

The OR was 2.16 that mean the risk its about more than two folds by CS. This is in agreement with Dani C et al (1999)<sup>(25)</sup>, and Levine EM. et al(2001)<sup>(49)</sup> who found an increase risk of general respiratory problems including TTN in neonate delivered after elective CS, compared with those delivered after a trial of labor, who found increase TTN by 2-3 folds than those by normal vaginal delivery. Thirteen patient (13%) of new born with TTN from asthmatic mothers. With OR of 3.586, with significant P value 0.023. There is significant association between maternal asthma and TTN. There is 15 patient (15%) of newborn with TTN from diabetic mothers. only 6 patient (6%) in control group from diabetic mothers. The OR was 2.765, with significant p value of 0.038. There is significant association between TTN and diabetic mothers, this study is compatible with Dani C et al (1999)<sup>(25)</sup>.

Only four patient (4%) of newborn from twin delivery, there was no significant association between TTN and twin...

The clinical features, usually resolve in first 72hours, so clinical features were significantly differed between those under 72hours than those above 72hours. Chest X Ray were done to all cases, at time of diagnosis and at 72hours of ages.

The radiological finding usually disappear before 72 hours in most of cases, were its significantly differed between those under 72h and those over 72h.

## CONCLUSIONS

1. The TTN is a disease of newborns below 72hours after birth and its responsible for a large number of hospitalization in NCU.
2. Males affected more than females and symptoms are prolonged in males.
3. There is significant association between maternal asthma and TTN.
4. There is significant association between mode of delivery and TTN specially in elective CS.

5. There is significant association between maternal diabetes and TTN.
6. The main risk factor for TTN are, elective caesarean section

### RECOMMENDATIONS

1. Anticipation of TTN in infant delivered by elective CS and with positive family history of asthma and diabetes.
2. This study also showed there is no significant association between birth weight and TTN. Birth weight is not risk factor for developing of TTN. This may be due the most of babies delivered in Iraq mothers having nutritional habit and absents of prenatal care.

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