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# From the Editor



Ahmad Husari (*Chief Editor*)  
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This is the fifth issue this year with various papers dealing with education, unique cases and research papers. A paper from Tikrit looked at assessment of the Educational Environment at Tikrit University College of Medicine (TUCOM). The authors attempt to measure students' perceptions of the educational environment of the TUCOM curriculum and to evaluate the internal consistency of the 50-item Dundee Ready Education Environment Measure (DREEM) Arabic version questionnaire. The 50-item DREEM Arabic version was found highly reliable. The authors concluded that the DREEM is a reliable and practical tool for assessing educational environment in Iraqi Medical Colleges. Certain problem areas were identified such as cheating, the support systems for students who become stressed, teaching that over-emphasized factual learning, teaching that is too teacher centered, and students' irritation with their teachers; these problems need to be examined more closely.

An observational, analytic, cross sectional study from Iraq attempted to estimate the prevalence of vitamin D deficiency among sample of pregnant women, correlate maternal and cord blood vitamin D deficiency and assess possible predictors of vitamin D deficiency. The mean 25OHD levels were 40.59nmol/l of the participants and 44.93nmol/l of their newborn. Vitamin D deficiency was noted in 40% and insufficiency in 38% of the participants whereas vitamin D deficiency and insufficiency were noted in 22% and 66% of their newborn respectively. There was a positive correlation between vitamin D levels in maternal and cord blood ( $r=0.762, p0.0001$ ). The authors concluded that vitamin D deficiency is high among pregnant women and their newborn. This public health problem needs urgent attention.

ER (Estrogen receptor) and PR (Progesterone receptor) are breast oncogene receptors that are important for the growth of some organs. A paper looked at the enhanced Accuracy and Reliability of ER and PR IHC Scoring Using ANN from Digital Microscope Images. A computer program was designed by the Author in Matlab language to study each type of receptors. The authors concluded that results of the methods are close to each other for ER and PR

receptors and statistical evaluation confirms that the program can be used as an objective method to confirm the first method. The program computing is better than the manual method for PO% computation because it is an objective method and shows results in a very accurate manner.

A paper from King Hussein Medical Centre looked at the role of Magnetic Resonance Imaging in diagnosing common disorders of the knee. A total number of 308 patients, presented with common symptoms of knee pain, and on whom they performed knee MRI to exclude meniscus or ligament injury of the knee. As a retrospectively review. Out of 308 patients on whom MRI was performed, in 179 patients (58.1%) of the examinations were positive. The authors concluded that MRI is sufficiently accurate in diagnosing common disorders of the knee, with preservation of knee arthroscopy for therapeutic tools preceded by MRI assessment.

Another paper looked at sub-cutaneous emphysema and pneumo-mediastinum in the perioperative period. Patients with sub-cutaneous emphysema of face and chest wall were observed within a few minutes after surgery. HRCT revealed sub-cutaneous emphysema and pneumo-mediastinum.

A paper from Jordan looked at transient neonatal pustular melanosis. The aim of the authors was to describe the epidemiology, clinical manifestation, differential diagnosis, therapy, and outcome of transient neonatal pustular melanosis. The present study was based on newly diagnosed cases presenting to the outpatient clinic of pediatric dermatology clinics at KHMC. The study included 114 patients. All subjects were products of hospital-based deliveries. The authors concluded that transients pustular melanosis is usually a self-limiting disease and without long term sequelae, to spare a healthy neonate with a benign transient condition and invasive evaluations for sepsis, harmful antibiotic therapy and prolonged hospitalization.

# The correlation between maternal and newborn serum 25-hydroxy - vitamin D in a sample of Iraqi women

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## ABSTRACT

**Objective:** To estimate the prevalence of vitamin D deficiency among a sample of pregnant women, correlate maternal and cord blood vitamin D deficiency and assessment of possible predictors of vitamin D deficiency.

**Method:** This observational, analytic, cross sectional study was conducted with 50 consecutive women in labor presenting with singleton term pregnancy at Al -Yarmouk teaching hospital during the period from April to October 2012. Data were recorded on an especial form. Maternal blood was taken before delivery and cord blood was taken at delivery. All blood samples (100) were analyzed for 25 hydroxy vitamin D levels.

**Results:** The mean 25OHD levels were (40.59nmol/l) of the participants and (44.93nmol/l) of their newborn. Vitamin D deficiency was noted in 40% and insufficiency in 38% of the participants whereas vitamin D deficiency and insufficiency were noted in 22% and 66% of their newborn respectively. There was a positive correlation between vitamin D levels in maternal and cord blood ( $r=0.762, p<0.0001$ ). Maternal vitamin D levels were significantly affected by sunlight exposure ( $p<0.016$ ).

**Conclusion:** Vitamin D deficiency is high among pregnant women and their newborn. This public health problem needs urgent attention.

**Key words:** Maternal vit. D. Cord blood vit. D

## Introduction

Over the past two decades, scientists, clinicians and researchers have generated a strong body of evidence to address the problem of vitamin D deficiency and provide advice for correcting its status among all ages, genders and racial/ethnic groups. Many studies, some randomized and some not, have suggested that a population with a higher vitamin D would be healthier overall. Generally, there are many important health benefits from vitamin D for both mother and fetus. However, new clinical research results over the past decade indicate that appropriate intake of vitamin D may provide greater health benefits than previously thought, benefits that include not only improved bone health, but other effects as well(1). Recent data suggest that 1,25(OH)<sub>2</sub>D aids implantation and maintains normal pregnancy. It also supports fetal growth through delivery of calcium, controls secretion of multiple placental hormones, and limits the production of proinflammatory cytokines (2). Maternal nutritional vitamin D status has a good effect on childhood bone mineral accrual and is important also for fetal “imprinting” that may affect neurodevelopment, immune function, and chronic disease susceptibility later in life, as well as soon after birth. (3, 4)

Also, maternal vitamin D insufficiency during pregnancy is significantly associated with offspring language impairment (5). Maternal vitamin D supplementation during pregnancy may reduce the risk of developmental language difficulties among children. Meanwhile, substandard vitamin D intake during pregnancy may lead to decreased birth weight(6). Moreover, maternal vitamin D deficiency in early pregnancy may be an independent risk factor for preeclampsia(7) and may be associated with odds of primary caesarean section. Merewood et al. found that 28% of women with serum 25(OH)D concentrations less than or equal to 37.5 nmol/L had a caesarean section, compared with only 14% of women with higher 25(OH)D concentrations ( $>37.5$  nmol/L)(8). Vitamin D deficiency has long been associated with poor bone development and has been identified as the cause of rickets. However, despite the availability of vitamin D and demonstration of its efficacy in preventing rickets, vitamin D deficiency rickets still exists as a public health problem with significant morbidity in the Middle East (9-11) and in many Asian countries, (12, 13) and has been reported with increasing prevalence in minority groups in North America (14, 15) and in immigrant populations in Europe, Australia and New Zealand. (16). In addition to rickets and other possible consequences of disturbed calcium homeostasis, epidemiological evidence suggests that lack of vitamin D supplements in infancy and early childhood may increase the incidence of type 1 diabetes.(17) In adults, new evidence(18) supports the role of vitamin D in maintaining innate immunity and in the prevention of certain disease states including autoimmune diseases, multiple sclerosis,(19-23)

systemic lupus erythematosus,(24) rheumatoid arthritis,(25,26) some forms of cancer (breast, ovarian, colon)(20) and type 2 diabetes and Alzheimer's disease.(27). Owing to increasing reports of vitamin D deficiency rickets among minority groups and the high prevalence of hypovitaminosis D in adults, especially in the United States and Canada,(28,29) reports of studies on vitamin D in the last decade have focused on these Western countries. However, many studies suggest that rickets is more common in Arab countries than is reported from the western countries. (30-32) Further, the prevalence of vitamin D deficiency is significantly higher in Arab women and children than in the white population. (33).

### Vitamin D physiologic components

Vitamin D is a prohormone that is derived from cholesterol. The nutritional forms of vitamin D include D3 (cholecalciferol), which is generated in the skin of humans and animals, and vitamin D2 (ergocalciferol), which is derived from plants; both forms can be absorbed in the gut and used by humans. Controversy exists as to whether D2 or D3 is more effective in maintaining circulating levels of vitamin D in non pregnant individuals, and specific data during pregnancy is unknown(14). The factors that influence endogenous production of cholecalciferol include time of day, season, latitude, length of sunshine exposure, percentage of body surface exposed to sunlight, and skin pigmentation. The amount of ultraviolet (UV) B radiation available for vitamin D synthesis is reduced in early morning, late evening, in winter and at high altitudes greater than 350 because these factors increase the ozone layer which absorbs more of the UV radiation required for vitamin D synthesis(14). In addition, inadequate exposure of the skin to sunshine by avoiding sunlight, wearing excessive clothing (especially wearing black clothing while outdoors), and use of sunscreens may reduce endogenous production of vitamin D(32). Compared with light-skinned persons, dark skinned persons are less efficient in producing vitamin D. In adults, the major dietary sources of ergocalciferol include fortified dairy products, orange juice and cereals as well as fish and fish oils(14). The dietary sources of vitamin D in infants are human milk and fortified formula in formula-fed infants. However, transplacental transfer of vitamin D is the major source of vitamin D for the fetus and during early infancy (33). The circulating 25-OHD is bound to vitamin D binding protein and transported to the kidneys where it is hydroxylated to produce 1-25-dihydroxyvitamin D- the most biologically active vitamin D metabolite. Other factors regulate the production of 1-25-dihydroxyvitamin D from the kidney; these include parathyroid hormone (PTH) and serum phosphorus and calcium. Decreases in serum concentrations of calcium and phosphorus and increases in serum concentrations of PTH stimulate synthesis of 1-25-dihydroxyvitamin D. 1-25-dihydroxyvitamin D increases intestinal absorption of calcium and phosphorus and decreases phosphorus excretion from the kidney; this maintains serum calcium and phosphorus homeostasis and is important for bone mineralization. In addition, an increase in serum PTH concentrations in response to low serum calcium concentration stimulates calcium and phosphorus mobilization from bone to maintain normal serum calcium and phosphorus

concentrations. Thus, through its active metabolites, vitamin D plays a major role in calcium and phosphorus homeostasis and in bone mineralization. (34)

### Subjects and Methods

Data came from a prospective pregnancy cohort study conducted in outpatient clinics at AL yarmouk teaching Hospital in Baghdad, Iraq, from April to October 2012. Women aged 14- 44 years who were carrying singleton infants, free of preexisting medical conditions, (none of the pregnant women who were under medications or affect of Ca or vitamin D status were included in the study), and planning to deliver at our Hospital, were eligible. After providing informed written consent, a detailed questionnaire was distributed to the mothers recruited, collecting information on their sociodemographic characteristics, use of topical sunscreens, and time spent outdoors during gestation (hours per week). Code numbers were given to every mother-newborn pair, and the mothers completed the questionnaires anonymously after the birth of their neonates. Sociodemographic factors examined were place of residence and maternal age, education, and occupation. Mothers were also asked about vitamin D and Ca supplement consumption during pregnancy. BMI were abstracted to ascertain self-reported pre-pregnancy weight and measured height. Pre-pregnancy BMI [weight (kg)/height(m)<sup>2</sup>] was based on measured height and maternal self-report of pre pregnancy weight at the first prenatal visit. Pre pregnancy BMI was categorized as lean (BMI 25), overweight (BMI 25.0-29.9), and obese (BMI >=30.0), ante partum and delivery events, and neonatal outcomes were recorded.

The study was approved by the ethics committee of the college of medicine Institutional Review Board. A total of 50 women enrolled in the study who had complete data on pregnancy outcomes, who had an index pregnancy delivered at term (37-42 wk) with no diagnosis of preeclampsia and an infant whose birth weight was deemed appropriate for its gestational age (10th percentile based on standards adjusted for gestational age, race, and sex).

### Blood Chemistry

Blood samples were obtained from mothers by antecubital venipuncture 30-60 minutes before delivery. Umbilical cord blood was collected immediately after clamping. Blood specimens were taken from the umbilical vein. Serum specimens were stored at 20°C until analysis. Neonates and mothers' samples were analyzed in the same run. Quantitation of serum [25(OH)D3] was performed using a commercial ELISA from Immunodiagnostic Systems and validated against an HPLC method (Euroimmun, Medizinsche-Labor Diagnostika, AG). The ELISA could detect 25(OH) D in the range of 5-300 nmol/L. The inter-assay CV for the ELISA was 10.3%. The relationship between serum 25(OH) D concentrations obtained from the ELISA compared with HPLC was as follows: slope  $\frac{1}{4}$  1.14, intercept  $\frac{1}{4}$  22,  $r^2$  0.901. We used this validation study to adjust the 25(OH) D concentrations obtained by ELISA to ensure better agreement with the HPLC data, as suggested by the manufacturer. The

intraassay percent coefficient of variation (CV) for this assay ranges from 2.4% at a 25(OH)D concentration of 71.8 ng/ml to 3.3% at a 25(OH)D concentration of 17.0 ng/ml. The inter-assay percent CV is 5.9% at a 25(OH)D concentration of 78.3 ng/ml and 6.7% at a 25(OH)D concentration of 14.0 ng/ml. The cutoff to define a normal circulating concentration of 25(OH)D is being debated. The same cutoffs were used for both women and neonates, because experts contend that the ideal healthy level of 25(OH) D3 is the same in infants as adults (6). In this study, a cut off of  $\geq 37.5$  nmol/L was used to derive the extent of vitamin D deficiency and 37.5 - 50.0 nmol/L. nmol/L to indicate insufficiency. Although there is no global consensus on the biochemical definition of vitamin D deficiency, a cut-off point of  $\geq 37.5$  nmol/L ( $\geq 15$  ng/mL) 25(OH)D is typically used to determine deficiency (35)

### Statistical Analysis

Descriptive data are presented as absolute number (n) and percentage (%) for qualitative variables and as median. One-way analysis of variance was performed to analyze the variance for a quantitative dependent (e.g., level of 25[OH]D) by a single factor categorized in three or more groups. The comparison of two groups of cases on one variance was performed by Student's t-test. Bivariate correlation was performed and Pearson's correlation coefficient (r) or Spearman's rho (non-normally distributed variables) were calculated.  $P < 0.05$  was considered significant. All statistical analyses were performed with the SPSS statistical software package (SPSS for Windows, 10; SPSS, Inc., Chicago, IL).

### Results

Baseline characteristics of the 50 women are presented in Table 1. Most women are housewives, 43 (86%), three of them were teachers, two doctors, two students, one nurse and one lawyer. Their mean age was  $27.1 \pm 6.7$ , mean BMI  $25.1 \pm 3.5$ . None of them were prescribed vitamin D supplements. No mother reported the use of topical sunscreens and all of them were of the same ethnic group and same skin color while the mean time spent outdoor exposing at least the face and extremities was 4.5 hours/week. Thirty four (68%) of the accouchement delivered vaginally and 16 (32%) by cesarean section. The mean gestational age was  $38.5 \pm 1.2$ . Of the neonates, twenty seven were males and twenty three were females. Their birth weight was  $3.486 \pm 0.436$ ; all were healthy term babies (Table 2). The mean maternal serum 25OHD was  $40.59 \pm 9.82$  nmol/l; no value was below 25.00 nmol/l, whereas the mean neonatal cord 25 OHD was  $44.93 \pm 12.66$  nmol/l with the lowest value of 9.77 nmol/l (Table 3, Figure 1). Maternal vitamin D deficiency (37.5nmol) was found in 40%; an additional 38% fell into the insufficient range (Figure 2). None of the participants had serum 25OHD levels less than 25 nmol/l. Of the neonates 31(62%) were insufficient and 11(22%) were vitamin D deficient. Age, occupation, parity and BMI were not significantly associated with serum 25OHD (Table 4). There was weak direct correlation between maternal Vitamin D and duration of sun exposure ( $r=0.340$ ;  $p=0.016$ ). There was significant correlation between neonatal Vitamin D and maternal age ( $p 0.035$ ) parity) ( $p 0.033$ ) and duration of sun exposure ( $p 0.008$ ) although the correlation was weak (Table 3 and 4). There was very strong direct correlation between maternal serum 25OH and neonatal cord blood 25HD ( $r=0.762$   $p 0.0001$ ) (Table 4, Figure 3)

### Discussion

This study has been carried out in AL-Yarmook teaching hospital in the capital Baghdad. Baghdad has a subtropical arid climate (Köppen climate classification BWh) and is, in terms of maximum temperatures, one of the hottest cities in the world. From June to August, the average maximum temperature is as high as 44 °C (111 °F) accompanied by blazing sunshine. Temperatures exceeding 50 °C (122 °F) in the shade are by no means unheard of. In Baghdad situated at an elevation of 34 meters above sea level, summer constitutes more than seven months of the year. In our study we found a high rate of vitamin D deficiency and insufficiency, 40% and 38% respectively, among term pregnant women. This was unexpectedly high, despite abundant sun exposure as evident by darkening of skin, and our study was carried out during summer (April to October) to avoid, although not eliminating, seasonal variation. This result is because all of the studied women were wearing veils and the majority of them were housewives with a mean of self reported sun exposure of 4.5 hours /week exposing their face and forearms. None of them had vitamin D measured during early pregnancy nor received vitamin D supplements and consuming a similar unfortified diet. This high rate of vitamin deficiency remained after control of other confounders. It is possible that some individuals incorrectly reported their sun exposure and/or body surface exposed. Despite this limitation, this population was clearly highly sun exposed as documented by darkening of exposed skin. In a study of 271 Lebanese women aged 30-50 years, wearing of veil was associated with low 25-OHD levels. Serum 25- OHD concentrations were negatively correlated with wearing a veil. Vitamin D deficiency (serum 25-OHD level  $< 12.5$  nmol/L) was present in 62% of veiled women compared with 24% of non veiled women.(36) Another study from the UAE compared the magnitude of clothing and duration of sunshine exposure among Arab women and Europeans residing in the UAE, because the extent of UV skin exposure depends on the degree of clothing and duration of sunshine exposure(9). In that study, 95%-100% of Arab women were likely to cover their forearms, legs and head while outdoors compared with 10%-30% of Europeans. Further, the average time spent in sunshine outdoors was 1.8 hours/week for Arab women compared with 4 hours/week by the European women. Mean serum 25-OHD concentrations were 5- to 7- fold higher in the Europeans than in Arabs. Both the magnitude of clothing and a UV skin exposure score (calculated by combining the duration of sunshine exposure and the magnitude of clothing) correlated with the serum 25-OHD concentrations indicating that a combination of heavy clothing that limits skin exposure to sunshine and a limited time of sunshine exposure while outdoors significantly increases the risk of hypovitaminosis D and should be addressed in efforts to improve endogenous production of vitamin D in Arab women.

We found vitamin D variation with maternal age, parity and duration of sun exposure but not with maternal BMI; maternal vitamin D increased with increasing age and parity and these factors may be related as increased parity associated with increasing age. High parity was found to be associated with hypovitaminosis D in some studies (36) and not in others(37).

There is some evidence that the relationship between obesity and 25(OH)D may vary by race/ethnicity. Recently,

		No	%
Maternal age (years)	<20	9	18.0
	20---24	9	18.0
	25---29	15	30.0
	30---34	10	20.0
	=>35	7	14.0
	Mean±SD (Range)	27.1±6.7	16-39
Maternal occupation	Housewives	43	86.0
	Governmental employee	7	14.0
Parity	Para 1	9	18.0
	Para 2	16	32.0
	Para 3	15	30.0
	Para 4	7	14.0
	Para 5 & more	3	6.0
	Mean±SD (Range)	2.6±1.2	1-6
BMI (Kg/m2)	18.5--24.9	27	54.0
	25--29.9	19	38.0
	=>30	4	8.0
	Mean±SD (Range)	25.1±3.5	19.9-33.8
Mode of delivery	Vaginal delivery	34	68.0
	CS	16	32.0
Average hours of sun exposure/week	2 hours---	27	54.0
	4 hours---	5	10.0
	6 hours---	13	26.0
	=>8 hours	5	10.0
	Mean±SD (Range)	4.5±2.9	2-18

Table 1: Maternal characteristics

		No	%
Neonatal sex	Male	27	54.0
	Female	23	46.0
Birth weight (Kg)	<3Kg	3	6.0
	3--	20	40.0
	3.5---	20	40.0
	=>4 Kg	7	14.0
	Mean±SD (Range) (Kg)	3.486±0.436	2.800-4.500
Gestational age (weeks)	37	12	24.0
	38	16	32.0
	39	11	22.0
	40	9	18.0
	41	2	4.0
	Mean±SD (Range) (weeks)	38.5±1.2	37-41

Table 2: Neonatal characteristics

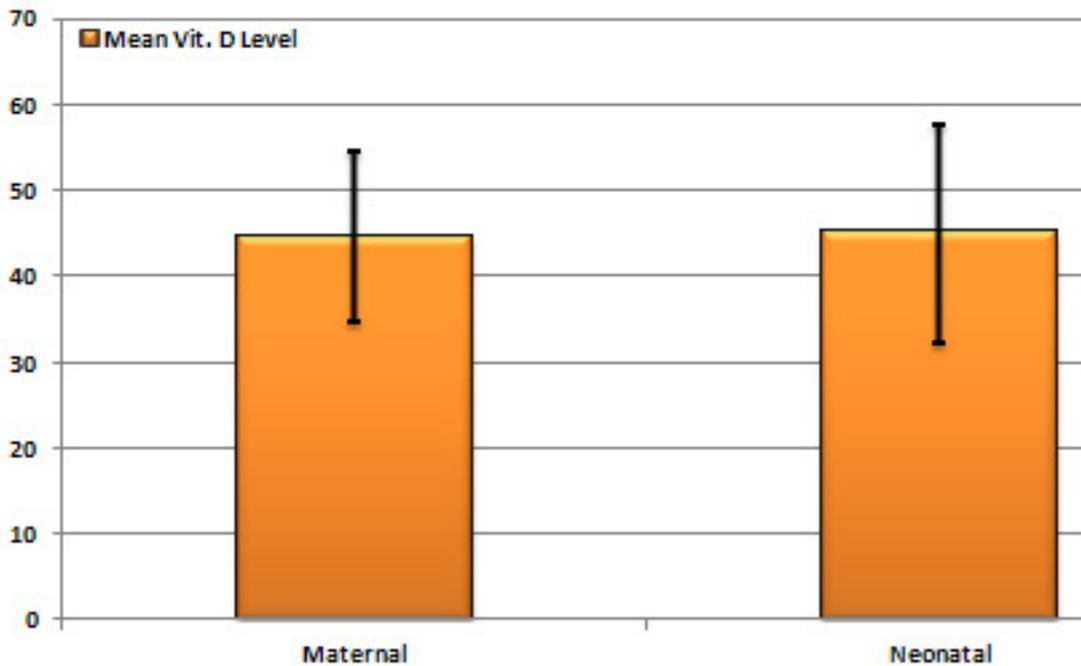


Figure 1: The mean Vitamin D level in maternal and neonatal blood

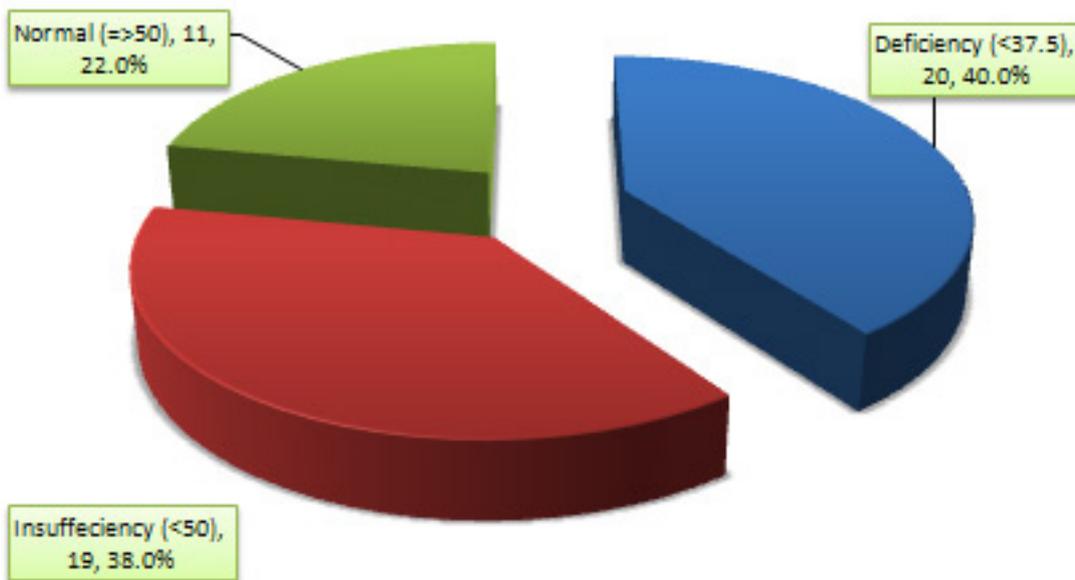


Figure 2: The level of Vitamin D in maternal blood

Looker (38) showed that the negative association between fat mass and 25(OH)D was significantly stronger in white women than in black women. Smaller studies have reported either no association between 25(OH)D and obesity in blacks (39) or a similar strong association in whites as in blacks (40). In our study there was no significant correlation between BMI and maternal vitamin D and our study groups are of the same race/ethnicity. However, our sample size may have limited our power to detect an interaction.

Most of the 25(OH) D measured in our cohort was 25(OH) D3 which is also synthesized by the skin after exposure to ultraviolet B radiation from the sun whereas 25(OH) D2 is not (41, 42). Vitamin D is present in few foods naturally (fatty fish, fish liver oils), used to fortify others (milk, breakfast

cereals, orange juice), and included in nutritional supplements (prenatal multivitamins). Vitamins D2 and D3 are both used in nutritional supplements and for food fortification (42).

The normal range of serum 25-OHD concentrations is controversial. In general, the lower limit of normal range (hypovitaminosis D) is defined as serum 25-OHD concentration of less than 25-37nmol/L (43). However, a higher cutoff level of serum 25-OHD concentration ( $< 50$ nmol/L) has been suggested, based on a recent physiologic study of the threshold serum 25-OHD concentrations required to maintain normal serum concentrations of PTH in adults. (44,45). Since it is generally accepted that the vitamin D status of the fetus and infant is dependent on the vitamin D status of the mother (42) we found a highly significant

		Maternal Vit. D (Mean±SD)	Neonatal Vit. D (Mean±SD)
<b>Maternal age (years)</b>	<20	33.47±8.12	34.14±11.16
	20---24	45.91±8.61	51.66±8.88
	25---29	41.61±11.74	44.85±15.75
	30---34	40.78±8.28	48.55±7.96
	=>35	40.47±7.47	45.17±10.03
	P value	0.104	0.035*
<b>Maternal occupation</b>	Housewives	41.04±10.04	44.21±13.21
	Governmental employee	37.86±8.51	49.36±7.91
	P value	0.432	0.323
<b>Parity</b>	Para 1	36.14±8.64	35.41±12.94
	Para 2	42.09±9.66	45.02±13.75
	Para 3	43.85±11.29	51.59±9.27
	Para 4	35.11±6.40	41.32±10.68
	Para 5&more	42.47±7.31	48.13±9.76
	P value	0.187	0.033*
<b>BMI (Kg/m2)</b>	18.5--24.9	38.03±9.16	42.14±13.01
	25--29.9	44.04±8.29	48.88±9.92
	=>30	41.50±17.37	44.97±19.86
	P value	0.121	0.209
<b>Mode of delivery</b>	Vaginal delivery	41.14±9.80	46.48±10.12
	CS	39.43±10.09	41.63±16.78
	P value	0.571	0.210
<b>Average hours of sun exposure/week</b>	2hours---	36.81±9.14	39.49±13.50
	4hours---	46.52±6.64	51.13±5.06
	6hours---	45.45±8.93	50.60±9.12
	=>8hours	42.46±11.60	53.34±8.08
	P value	0.022*	0.008*
<b>Neonatal sex</b>	Male	41.58±10.00	45.26±13.13
	Female	39.43±9.71	44.54±12.37
	P value	0.447	0.843
<b>Birth weight (Kg)</b>	<3Kg	37.40±10.64	40.51±13.66
	3--	41.95±8.98	45.49±11.21
	3.5---	40.61±10.36	45.83±13.41
	=>4 Kg	38.04±11.67	42.68±16.15
	P value	0.771	0.875
<b>Gestational age (weeks)</b>	37	44.10±8.47	48.67±8.69
	38	36.44±8.63	41.92±11.65
	39	46.02±7.12	47.71±15.88
	40	39.88±11.99	45.26±13.35
	41	26.20±0.28	29.81±13.77
	P value	0.011	0.257

\*Significant using ANOVA test for difference among more than two independent means or Student-t-test for difference between two independent means at 0.05 level

**Table 3: Maternal & Neonatal Vitamin D level according to different parameters**

correlation between maternal and cord blood vitamin D and a high prevalence of neonatal vitamin deficiency and insufficiency of 62% and 22% respectively with the lowest value of 9.7 nmol/l which was not affected by weight, sex of neonate or mode of delivery. Typically, the vitamin D status of Arab mothers and their infants at delivery was found to be low and the prevalence of hypovitaminosis D was high, but the rate depended on the definitions of hypovitaminosis D

and vitamin D deficiency used in the study. In a study of 119 Saudi mothers and their newly born infants, the mean serum concentrations of 25-OHD were 12, 13.8, and 17.5nmol/L in the lower, middle and upper-class women respectively(30). The mean umbilical cord serum 25-OHD concentration of 7.5nmol/L was very low and was similar in all the 3 classes. Several authors had suggested that a decrease in the endogenous production of vitamin D is responsible for

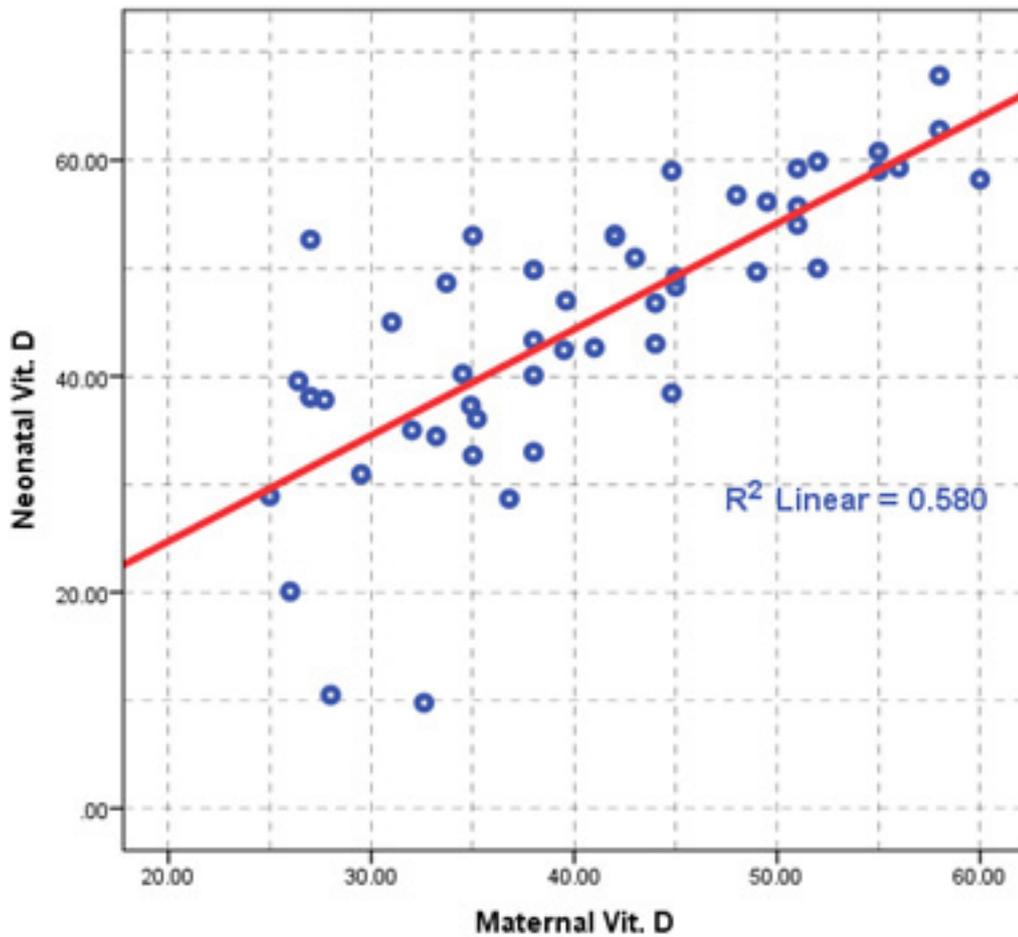


Figure 3: There is highly significant strong direct correlation ( $r=0.762$ ;  $P=0.0001$ )

		Maternal Vit. D	Neonatal Vit. D
Maternal age (years)	r	0.072	0.180
	P	0.620	0.210
Parity	r	0.041	0.214
	P	0.777	0.136
BMI (Kg/m <sup>2</sup> )	r	0.211	0.175
	P	0.141	0.224
Average hours of sun exposure/week	r	0.340*	0.420**
	P	0.016	0.002
Birth weight (Kg)	r	0.0001	0.009
	P	0.999	0.949
Gestational age (weeks)	r	-0.146	-0.137
	P	0.313	0.343
Maternal Vit. D	r	-	0.762**
	P		0.0001

\*Correlation is significant at the 0.05 level. \*\*Correlation is significant at the 0.01 level

Table 4: The correlation of Maternal and neonatal Vitamin D with different variables

the high prevalence of hypovitaminosis D and vitamin D deficiency in Arab women. Low dietary intake of vitamin D has been implicated as a contributing factor in only a few studies. There are a growing number of reports on the high prevalence of low circulating serum 25(OH) D concentrations linked to restricted sunlight exposure and inadequate vitamin D intake in women of childbearing age and in children in many countries. International comparison of the prevalence of vitamin D deficiency is difficult because of variation in the definition of vitamin D deficiency in reported studies. It is generally agreed that a serum 25(OH)D concentration, 25 nmol/l is associated with rickets and osteomalacia. In adults, a serum 25(OH)D concentration, 50-80 nmol/l is now considered insufficient for optimal bone health(46). In the US, 45% of African American women have frank vitamin D deficiency as defined by a serum 25(OH)D concentration ,37 nmol/l (15 ng/ml)(47). In Turkey, women wearing traditional dress outdoors have a mean serum 25(OH)D concentration of 32 nmol/ l compared with a mean of 9 nmol/l among those who are completely covered(48). Reports indicate that upwards of 26-84% of women in Lebanon (36) Saudi Arabia (45) the United Arab Emirates (UAE)(49) Bangladesh (50) Japan (51) and Finland (52) have serum25(OH)D concentrations,25 nmol/ l (10 ng/ml). Maternal vitamin D deficiency during pregnancy also was documented in a number of studies two decades ago(53). In more recent reports, 18% of pregnant women in the UK(3), 25% in the UAE(54), 80% in Iran(55), 42% in northern India (56), 61% in New Zealand (57) and 60-84% of pregnant non-Western women in the Netherlands(23) have been shown to have serum 25(OH)D concentrations ,25 nmol/l. This raises the concern that infants are entering the world with a vitamin D deficit that begins in utero.(58) This concern is based on the strong relationship between maternal and fetal (cord blood) circulating 25(OH)D levels, that have demonstrated a high prevalence of vitamin D deficiency in mother-infant pairs at birth(59). The significance of maternal deficiency during pregnancy is that the fetus is developing in a state of hypovitaminosis D, which likely has significant effects on innate immune function and fetal and childhood bone development.(60) Assessing vitamin D intake has become increasingly important because of the growing recognition that humans might not form adequate supplies of vitamin D from exposure to sunlight alone. Because several factors (such as clothing, skin color, and latitude) can impair sunlight-induced cutaneous vitamin D synthesis, many people must rely on dietary sources to satisfy their vitamin D requirements. The few studies of dietary vitamin D intake show that Arab women lack adequate intake of vitamin D. The factors that contribute to low dietary vitamin D intake were avoidance of milk, and consumption of non fortified dairy products(33). All the reported studies indicate that the major risk factor for high prevalence of vitamin D deficiency in Arab women and other mothers of Middle Eastern origin is a decrease in endogenous vitamin D synthesis. Inadequate dietary vitamin D intake and possibly less efficient synthesis of vitamin D among some dark-skinned Arab women are contributory factors. The high prevalence of vitamin D deficiency in infants is a combined effect of maternal vitamin D deficiency and prolonged breast feeding without vitamin D supplementation. Many factors have contributed to the

continuing high prevalence of hypovitaminosis D in Arab women and infants. First, there is a lack of awareness of the magnitude of hypovitaminosis D and its effects on health owing to delay in the clinical manifestation of vitamin D deficiency. Second, many physicians fail to follow the general recommendation of prescribing vitamin D supplementation to breastfeeding infants whose mothers are at risk of hypovitaminosis D(61).

Finally, there is a continuing challenge regarding how to effect changes in women's lifestyles to increase sunshine exposure and endogenous vitamin D production. As indicated in many recent reviews and editorials, it is time to take action to eliminate hypovitaminosis D and vitamin D deficiency (62, 63). Public health education activities are urgently needed to encourage modest sunshine exposure. Although the optimal vitamin D requirement during pregnancy and lactation has not been established, Vitamin D supplementation, however, remains the best option for improving vitamin D status and eliminating hypovitaminosis D in Arab women and children until modifications in lifestyle can be achieved to improve endogenous vitamin D synthesis. Vitamin D supplementation programs should be instituted and made accessible. In conclusion, all of the studies to date suggest that hypovitaminosis D and vitamin D deficiency may be an unrecognized public health problem among Arab women and their infants. Community-based studies using generally accepted definitions are needed to establish the magnitude of the problem. In view of the morbidity associated with vitamin D deficiency in mothers and growing infants, there is a compelling need to take public health measures to improve the vitamin D status of Arab women and infants. This should include wide spread vitamin D supplementation, modest skin sunshine, increase in food fortification with vitamin D, and an awareness among the public and physicians on the urgent need to improve vitamin D intake. Future research should focus on the appropriate daily dietary vitamin D intake that will prevent hypovitaminosis D if sunshine exposure is limited. How adequate are the current recommendations to prevent vitamin D deficiency in mothers and children? Although vitamin D supplementation is effective in preventing vitamin D deficiency, the optimal vitamin D requirement in women and children is still unknown. Published data indicate that vitamin D deficiency may be an unrecognized public health problem in women, nursing mothers and children in many populations, at least in populations where sun exposure in women and children is severely limited. There is an urgent need to determine the optimal dose of vitamin D to ensure vitamin D sufficiency in pregnant and lactating women when sun exposure is inadequate. A strategy to prevent vitamin D deficiency in infants through maternal supplementation which would achieve the double effect of preventing vitamin D deficiency in both mothers and children may be a way forward and needs further study. Strategies to prevent vitamin D deficiency and achieve adequate intake of vitamin D and calcium in women and throughout childhood would not only prevent rickets but may also reduce the risk of osteoporosis as well as other long latency disease processes that have been associated with vitamin D deficient states in adults. This may be one of the more important preventive public health initiatives. The time for action is now.

## References

1. Souberbielle JC, Body JJ, Lappe JM, Plebani M, Shoenfeld Y, Wang TJ, et al. Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice. *Autoimmun Rev*. 2010;9:709-15.[PubMed]
2. Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects on pregnancy and the placenta. *Placenta*. 2010;31:1027-34. [PMC free article][PubMed]
3. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, et al. Maternal vitamin D status during pregnancy and childhood bone mass at 9 years: A longitudinal study. *Lancet*. 2006;367:36-43.[PubMed]
4. McGrath J. Does "imprinting" with low prenatal vitamin D contribute to the risk of various adult disorders? *Med Hypotheses*. 2001;56:367-71.[PubMed]
5. Whitehouse AJO, Holt BJ, Serralha M, Holt PG, Kusel MMH, Hart PH. Maternal serum vitamin D levels during pregnancy and offspring neurocognitive development. *Pediatrics*. 2012;129:485-93.[PubMed]
6. Mannion CA, Gray-Donald K, Koski KG. Association of low intake of milk and vitamin D during pregnancy with decreased birth weight. *CMAJ*. 2006;174:1273-7. [PMC free article][PubMed]
7. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. *J Clin Endocrinol Metab*. 2007;92:3517-22.[PubMed]
8. Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary caesarean section. *J Clin Endocrinol Metab*. 2009;94:940-5. [PMC free article][PubMed]
9. Dawodu A, Absood G, Patel M, Agrawal M, Ezimokhai M, Abdulrazzaq, et al. Biosocial factors affecting vitamin D status of women of childbearing age in the United Arab Emirates. *J Biosoc Sci* 1998; 30:341-7
10. Karrar ZA. Vitamin D deficiency rickets in developing countries. *Ann Trop Paediatr* 1998; 18 Suppl: S89-92.
11. Nozza JM, Rodda CP. Vitamin D deficiency in mothers of infants with rickets. *Med J Aust* 2001; 175:253-5.
12. Shaw NJ, Pal BR. Vitamin D deficiency in UK Asian families: activating a new concern. *Arch Dis Child* 2002;86:147-149.
13. Fraser DR. Vitamin D-deficiency in Asia. *J Steroid Biochem Mol Biol* 2004; 89-90:491-5.
14. Kreiter SR, Schwartz RP, Kirkman HN, Jr., Charlton PA, Calikoglu AS, Davenport ML. Nutritional rickets in African American breast-fed infants. *J Pediatr* 2000; 137:153-7.
15. Nesby-O'Dell S, Scanlon KS, Cogswell ME, Gillespie C, Hollis BW, Looker AC, Allen C, Dougherty C, Gunter EW, Bowman BA. Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: third National Health and Nutrition Examination Survey, 1988-1994. *Am J Clin Nutr* 2002; 76:187-92
16. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *Cmaj* 2002; 166:1517-24
17. Zipitis CS, Akobeng AK. Vitamin D supplementation in early childhood and risk of type 1 diabetes: a systematic review and meta-analysis. *Arch Dis Child* 2008;93:512-7
18. Billiet L, Furman C, Larigauderie G, Copin C, Page S, Fruchart JC, Brand K, Rouis M: Enhanced VDUP-1 gene expression by PPAR gamma agonist induces apoptosis in human macrophage. *J Cell Physiol* 2008, 214(1):183-191
19. Danescu LG, Levy S, Levy J. Vitamin D and diabetes mellitus. *Endocrine* 2009;35:11-7.
20. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease [review]. *Am J Clin Nutr* 2004;80(6 Suppl):1678S-1688S
21. Liu PT, Stenger S, Li H, Wenzel L, Tan BH, Krutzik SR, et al. Toll-like receptor triggering of vitamin D-mediated human antimicrobial response. *Science* 2006;311:1770-3.
22. Ebers GC. Environmental factors and multiple sclerosis. *Lancet Neurol* 2008;7:268 -77.
23. Munger KL, Levin LI, Hollis BW, Howard NS, Ascherio A. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. *JAMA* 2006;296:2832-8.
24. Smolders J, Damoiseaux J, Menheere P, Hupperts R. Vitamin D as an immune modulator in multiple sclerosis, a review. *J Neuroimmunol* 2008;194:7-17.
25. Siam A/R, Hammoudeh M, Khanjer I, Bener A, Sarakbi H, Mehdi S. Vitamin D deficiency in Rheumatology clinic practice in Qatar. *Qatar Med J*. 2006;15:49-51.
26. Cutolo M, Otsa K, Laas K, Yprus M, Lehtme R, Secchi ME, Sulli A, Paolino S and Seriole B: Circannual vitamin D serum levels and disease activity in rheumatoid arthritis: Northern versus Southern Europe. *Clin Exp Rheumatol* 24: 702-704, 200
27. Oudshoorn C, Mattace-Raso FU, van der Velde N, Colin EM, van der Cammen TJ. Higher serum vitamin D3 levels are associated with better cognitive test performance in patients with Alzheimer's disease. *Dement Geriatr Cogn Disord* 2008;25:539- 43.
28. Weisberg P, Scanlon K, Li R, Cogswell ME. Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003. *Am J Clin Nutr* 2004; 80(6 Suppl):1697S-1705S.
29. Binet A, Kooh SW. Persistence of vitamin D deficiency rickets in Toronto in the 1990s. *Can J Public Health* 1996;87:227-30.
30. Serenius F, Elidrissy AT, Dandona P. Vitamin D nutrition in pregnant women at term and in newly born babies in Saudi Arabia. *J Clin Pathol* 1984; 37:444-7.
31. Markestad T, Elzouki A, Legnain M, Ulstein M, Aksnes L. Serum concentrations of vitamin D metabolites in maternal and umbilical cord blood of Libyan and Norwegian women. *Hum Nutr Clin Nutr* 1984; 38:55-62.
32. Dawodu A, Agarwal M, Hossain M, Kochiyil J, Zayed R. Hypovitaminosis D and vitamin D deficiency in

- exclusively breast-feeding infants and their mothers in summer: a justification for vitamin D supplementation of breast-feeding infants. *J Pediatr* 2003; 142:169-7
33. Hollis BW, Wagner CL. Assessment of dietary vitamin D requirements during pregnancy and lactation. *Am J Clin Nutr* 2004;79:717-26.
  34. Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: a longitudinal study. *Am J Clin Nutr* 1995;61:514-23.
  35. Hathcock JN, Shao A, Vieth R, Heaney R. Risk assessment for vitamin D. *Am J Clin Nutr*. 2007;85:6-18.[PubMed]
  36. Gannage-Yared MH, Chemali R, Yaacoub N, Halaby,. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *J Bone Miner Res* 2000;15:1856-62
  37. Moghraby SA, Al Shawaf T, Akiel A, Sedrani SH, el Idrissy AT, Al-Meshari AA. Parity and vitamin D metabolites. *Ann Trop Paediatr* 1987; 7:210-3.
  38. Looker AC. Body fat and vitamin D status in black versus white women. *J Clin Endocrinol Metab*. 2005;90:635-40.
  39. Epstein S, Bell NH, Shary J, Shaw S, Greene A, Oexmann MJ. Evidence that obesity does not influence the vitamin D-endocrine system in blacks. *J Bone Miner Res*. 1986;1:181-4
  40. Parikh SJ, Edelman M, Uwaifo GI, Freedman RJ, Semega-Janneh M, Reynolds J, Yanovski JA. The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. *J Clin Endocrinol Metab*. 2004;89:1196-9.
  41. Specker B. Vitamin D requirements during pregnancy [review]. *Am J Clin Nutr* 2004;80(6 Suppl):1740S-1747S.
  42. Ghannam NN, Hammami MM, Bakheet SM, Khan AB. Bone mineral density of the spine and femur in healthy Saudi females: relation to vitamin D status, pregnancy, and lactation. *Calcif Tissue Int* 1999;65:23-8
  43. Van der Meer IM, Karamali NS, Boeke AJ, Lips P, Middelkoop BJ, Verhoeven I, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr*. 2006;84:350-3.
  44. Stroud ML, Stilgoe S, Stott VE, Alhabian O, Salman K. Vitamin D: A review. *Aust Fam Physician*. 2008;37:1002-5.[PubMed]
  45. Hollis BW, Wagner CL. Nutritional vitamin D status during pregnancy: reasons for concern. *CMAJ* 2006;174(9):1287-90.
  46. Calvo MS, Whiting SJ, Barton CN. Vitamin D fortification in the US and Canada: current status and data needs. *Am J Clin Nutr* 2004;80(suppl): 1710S-6S
  47. Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D; National Academies Press: Washington, DC, USA, 2011.
  48. Alagöl F, Shihadeh Y, Boztepe H, Azizlerli H, Sandalcıy O. Sunlight exposure and vitamin D deficiency in Turkish women. *J Endocrinol Invest* 2000; 23: 173-177
  49. Saadi HF, Nagelkerke N, Benedict S, Dawodu A, Afandi BO, Zayed R, et al. Predictors and relationships of serum 25 hydroxyvitamin D concentration with bone turnover markers, bone mineral density, and vitamin D receptor genotype in Emirati women. *Bone* 2006;39(5):1136-43.
  50. Islam MZ, Akhtaruzzaman M, Lamberg-Allardt C. Hypovitaminosis D is common in both veiled and non-veiled Bangladeshi women. *Asia Pac J Clin Nutr* 2006;15:81-7.
  51. Nakamura, K., Nashimoto, M., Okuda, Y., Ota, T., & Yamamoto, M. (2002). Fish as a major source of vitamin D in the Japanese diet. *Nutrition*, 18(5), 415-416.
  52. Lamberg-Allardt CJ, Outila TA, Karkkainen MU, et al. Vitamin D deficiency and bone health in healthy adults in Finland: could this be a concern in other parts of Europe? *J Bone Miner Res* 2001;16:2066-73
  53. Specker BL, Tsang RC. Vitamin D in infancy and childhood: factors determining vitamin D status. *Adv Pediatr* 1986; 33:1-22
  54. Dawodu A, Wagner CL. Mother-child vitamin D deficiency: an international perspective. *Arch Dis Child* 2007;92:737-40.
  55. Bassir M, Laborie S, Lapillonne A, Claris O, Chappuis MC, Salle BL. Vitamin D deficiency in Iranian mothers and their neonates: a pilot study. *Acta Paediatr* 2001;90:577-9.
  56. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr* 2005;81:1060-4.
  57. Judkins A, Eagleton C. Vitamin D deficiency in pregnant New Zealand women. *N Z Med J* 2006;119(1241):U2144.
  58. Hollis BW, Pittard WB. Evaluation of the total fetal/maternal vitamin D relationships at term: evidence for racial differences. *J Clin Endocrinol Metab* 1984;59:652-7.
  59. Nicolaidou P, Hatzistamatiou Z, Papadopoulou A, Kaleyias J, Floropoulou E, Lagona E, et al. Low vitamin D status in mother-newborn pairs in Greece. *Calcif Tissue Int* 2006;78(6):337-42
  60. Pawley N, Bishop NJ. Prenatal and infant predictors of bone health: the influence of vitamin D [review]. *Am J Clin Nutr* 2004;80(6 Suppl):1748S-1751
  61. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am J Clin Nutr* 2004;79:362-71.
  62. Vieth R, Fraser D. Vitamin D insufficiency: no recommended dietary allowance exists for this nutrient. *Cmaj* 2002; 166:1541-2.
  63. Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest* 2006;116:2062-72.

# Enhanced Accuracy and Reliability of ER and PR IHC Scoring Using ANN from Digital Microscope Images

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## ABSTRACT

**Background:** ER (Estrogen receptor) and PR (Progesterone receptor) are breast oncogene receptors that are important for the growth of some organs. Their statuses for breast cancer patients are vital to determine chemical therapy for the patients after surgical removal of cancer.

**Methods:** A computer program designed by the author in Matlab language to study each type of receptors (nearly 10 slide images studied for each one). The program used pixel color classification techniques by using Artificial Neural Network (ANN).

**Results:** Some image resizing, re-dimensioning, and enhancing are done by Photoshop program which aimed to obtain better results of Proportion Observation percent (PO%). The PO% was estimated for ER and PR receptors by two methods; routine test which was done by a pathologist (manual scoring), and by the designed program used in this study (computer scoring).

**Conclusions:** Results of the methods are close to each other for ER and PR receptors and statistical evaluation confirms that the program can be used as an objective method to confirm the first method. The program computing is better than the manual method for PO% computation because it is an objective method and shows results in a very accurate manner.

**Key words:** ER, PR, HER2 receptor, Image processing

## Introduction

Breast cancer is the leading female cancer in Europe and in the USA and amongst the cancer types with high incidence in the rest of the world. In the UK and USA, approximately one in every ten women will contract the disease in their lifetime and it is amongst the leading cause of death in the female population in industrialized countries [Mansel et al., 2007].

The molecular classification of tumors often helps to establish their aggressiveness and the molecular status which generally has a major effect on patient morbidity and mortality. Some biomarkers which are commonly tested include estrogen, progesterone, and Her-2 receptors.

The researcher Gown considers ER as a weak prognostic marker of clinical outcome in breast cancer, but a strong predictive marker for response, for example, to Tamoxifen-based (TAM) therapy [Gown, 2008]. Koshnod suggested that ER negativity in some of his patient cases is correlated with an increased tumour growth rate [Khoshnoud, 2008]. Bernoux and others, in 1998, have shown that ER/PR status affects endocrine therapy. They concluded that patients with ER-PR+ tumors are mainly perimenopausal and tend to have a better outcome than ER-PR- patients. On the basis of ER status alone these patients are generally not considered as candidates for endocrine therapy. The presence of PR may lead one to reconsider this modality of treatment [Bernoux et al., 1998]. A high proportion of breast tumors in men are estrogen receptor-positive (in their review 77%) and progesterone receptor positive (76%) as showed by Hakan, in 2000. Breast tumors in men often respond favorably to endocrine manipulation, including testicular ablation or antiestrogen therapy. Thus, the hormone receptors in these tumors can be functionally active and used for therapeutic intervention [Hakan, 2000].

Yu and others, in (2008), also studied the ER/PR status related to age of the patients. Patients with ER-/PR+ tumors were younger than those with ER+/PR+ tumors ( $P=0.021$ ), and were mainly premenopausal ( $P=0.013$ ). ER-/PR+ patients were related to more involved lymph nodes and later stage. Although patients with ER-/PR+ tumors are generally considered as candidates for endocrine therapy clinically, the ER-/PR+ group gains less benefits from adjuvant TAM treatment than ER+/PR+ group [Yu et al., 2008]. Liu and others, in (2010), have shown the importance of determining PR status for selecting best hormone therapy. Furthermore the identification of the ER-/PR+ cohort allows them the option for hormonal therapy [Liu et al., 2010].

Digital images, from their vital role in the early detection and treatment, become subject to a lot of research to try to analysis them and get the most possible information from them. Image processing techniques used to reach the

important target. Biomedical image processing has experienced dramatic expansion, and has been an interdisciplinary research field attracting expertise from applied mathematics, computer sciences, engineering, statistics, physics, biology and medicine [Zhu, 2003]. One of the important techniques in image analyzing is artificial neural network.

It is believed that neural networks will have extensive application to biomedical problems in the next few years. Already, it has been successfully applied to various areas of medicine, such as diagnostic systems, biochemical analysis, image analysis, and drug development. The benefits of using ANNs are that they are not affected by factors such as fatigue, working conditions and emotional state [Siganos, 2011].

Image segmentation, which will be done by ANN technique, is one of the key problems in Histopathological image analysis, since most of the subsequent analysis steps rely on the accuracy and the precision of the segmentation step. In general, segmentation of histopathology images aims for the partitioning of the tissue content into distinct structures of interest (e.g., cytological components, follicles or fibers, etc.). A common approach to the image segmentation problem in histopathology imagery is to model image segmentation as a data clustering problem. The challenge associated with feature space clustering approaches is the choice of a relevant feature space (e.g., color, texture, etc.). One can show that within a well-defined feature space consisting of color and texture, clustering based image segmentation provides promising results [Sertel, 2010].

Neural networks have wide applications in recognizing diseases and hence they are critical in the field of medicine. Thiran and Macq presented a method for automatic recognition of cancerous tissues from an image of a microscopic section. Based on the shape and the size analysis of the observed cells, this method provides the physician with non-subjective numerical values for four criteria of malignancy. From the values of the extracted criteria, an automatic classification of the image (cancerous or not) is finally operated [Thiran and Macq, 1996].

It is necessary to perform surgical biopsies to obtain tissue for histologic examination and diagnosis throughout molecular assays. Not only do biopsy sections lead to clinical diagnoses, but more importantly, they can indicate appropriate routes of treatment and expectation of morbidity/mortality. Therefore, great significance is attributed to biopsies and those who interpret them (i.e., pathologists). Although the scoring systems are often sophisticated, it is nevertheless surprising that interpretations of tissue parameters can vary greatly between pathologists. Indeed, pathologists come to complete agreement as low as 9% of the time. A qualitative skill dependent on the experience of the practitioner, tissue grading is sufficiently clinically significant that normalization among all specimens should be essential because of the risk that a slightly incorrect qualitative evaluation could lead to lethal consequences as therapeutic regimens are selected on the basis of such assessments. Therefore, impartial quantitative

histological evaluation procedures may be desirable prior to samples reaching a pathologist [Smith, 2006].

The present work aimed to design and program an image processing code in MATLAB which uses Artificial neural network to distinct positive and negative stained cells from breast cancer tissue slides and to count both type of cells individually and determine Proportion Observation percent (PO%) which is important to determine IHC score.

## Materials and Methods

Digital microscopes were used to capture images (saved in Jpg format) for IHC slides composed of a Microscope type Biolab-1007, Altay supplied with Digital Camera Eyepiece (MDCE-5A) that has a 1/3" image sensor (CMOS Sensor, 1.3 Mega Pixel).

Slide images were resized and re-dimensioned to smaller ones with enhanced clarity using Photoshop program. Color images convert to gray scale images where brown colors (positive cancer cells) convert to black and negative cancer cells to less black color by two codes written in Matlab 7.11.0 (R2010b) using ANN techniques. The first code selects three different colors for positive cells (brown), negative cells (blue) and background (mostly white) and it converts the image into a new matrix with 3 rows by n columns. The second code uses Levenberg-Marquardt back-propagation Artificial neural network (LM BP ANN) {Figure 1 for diagram of ANN} to classify color pixels by using newff function.

The input vector is composed of 3 elements corresponding to the RGB color vector of pixels. Two hidden layers are determined empirically to be 3-10 neurons and the output layer consists of one neuron. In addition, the transfer functions of hidden and output layers are tan-sigmoid and linear, respectively. For the training of neural networks, the target is assigned to be [-1 0.5 1]. The networks are trained using the Levenberg-Marquardt (trainlm) algorithm. The training stops when the maximum number of epochs reaches 4000 or the mean square error is less than  $1 \times 10^{-17}$ . Finally the produced matrix is reshaped to gray scale image. The third code takes the output gray scale image from the second code and puts the positive cells in one image (black regions) and negative cells (less black) to another one (see Figure 2 for flowchart of third code).

For counting cells, a cell with minimum area is selected and the diameter of it is measured and it then computes the area of that cell as a circle. It counts the total number of P cells and N cells and adds the two images and computes PO% using following equation:

$$PO\% = \frac{P \text{ cells}}{All \text{ cells}} \cdot 100$$

Manual total counting of P- and N- cells for ER and PR receptors were done by adding grids to the image, and choosing 5 fields randomly. Then, it takes the average of P- and N-cells for the five fields and multiplies the average of

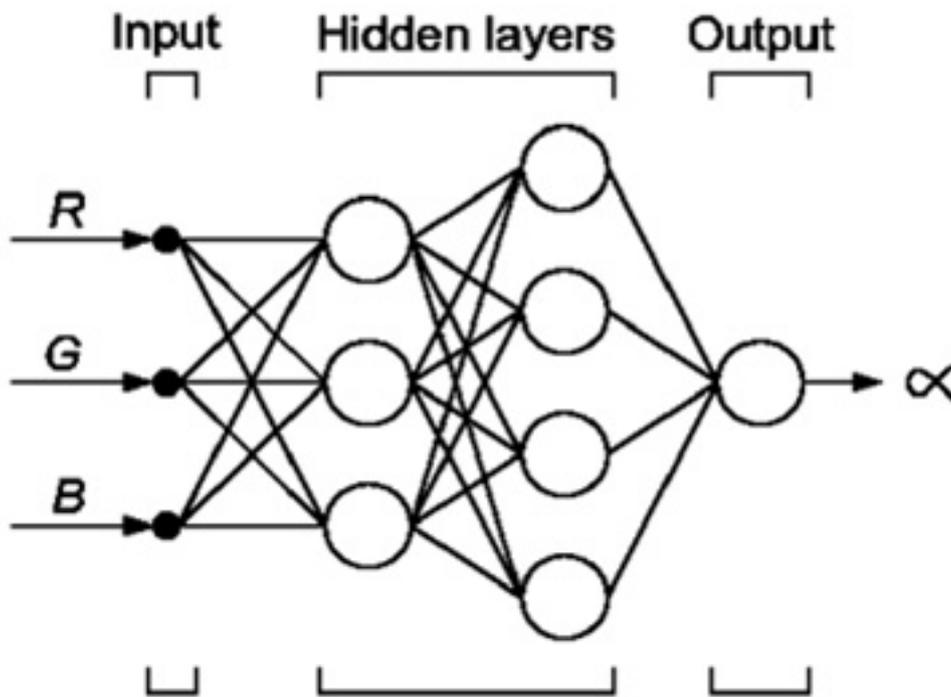


Figure 1:  
Diagram of BP ANN

each type by the total number of fields. This method is repeated to have three values of total P- and N-cells in the images. Finally, use Eq.(1) to calculate PO%.

ER and PR receptors are steroid receptors localizing to the nucleus. Positive ER and PR results are further qualified using a rapid semiquantitative H score ranging from 0 to 8 that takes into account both the intensity of staining and proportion of tumor cells staining positive for ER and PR receptors with appropriate cutoff values for treatment of advanced disease.

The score for proportion staining (PS) is: 0 score = denotes no nuclear staining, 1 score = 1%, 2 score = 1%-10%, 3 score = 11%-33%, 4 score = 34%-66%, 5 score = 67%- 100% nuclei staining. Score for staining intensity (SI) is determined as: 0 intensity = denotes no nuclear staining, 1 intensity = weak staining, 2 intensity = moderate staining, 3 intensity = strong staining. The two scores are added and describe according to their values that: score 0 indicates endocrine treatments or tamoxifen will definitely not work and such patients should receive an alternative first-line treatment; score 2-3 indicates a 20% chance of response to endocrine treatment; score 4-6 indicates a 50% chance of response to endocrine treatment; score 7-8 indicates a good (75%) chance of response to endocrine treatment [Huang et al., 1999; Patil et al., 2011]. Total score represents positive tumors if it equals or exceeds 3 [Krecsák et al., 2011].

## Results

The P-cells, N-cells, PO% were listed manually and the Matlab codes for both receptors in Tables 1 to 3. Table 1 showed counting of P-, N-cells and PO% for ER which were stained by DAB method. But for the same parameter for PR that was stained by DAB is shown in Table 2 and PR stained by AEC method is shown in Table 3. DAB staining, gives the

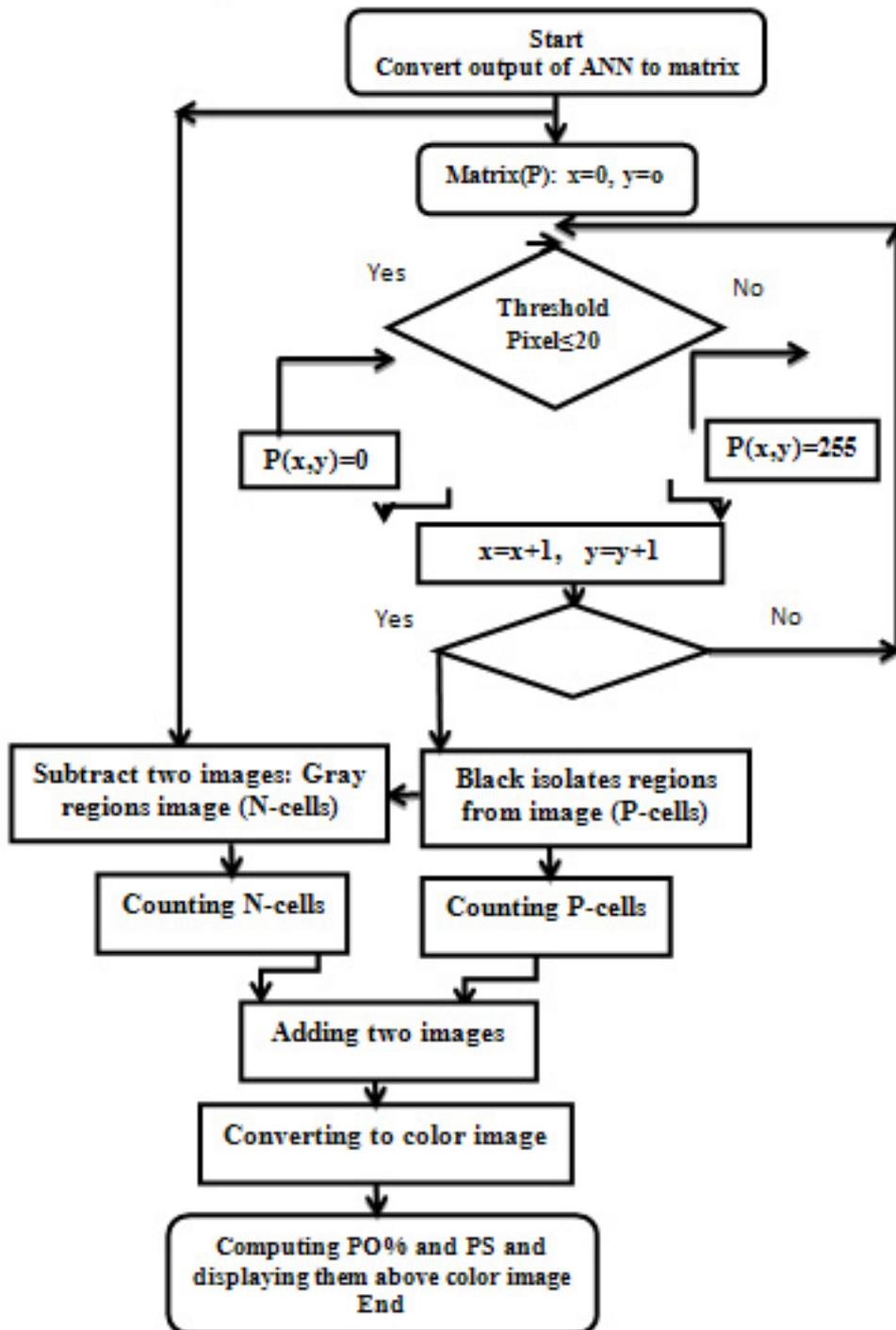
positive cells a brown color and negative cells with blue but the second method, ACE staining, gives the positive with red color for cell membrane and blue for nucleus. The codes give us total P-cells and N-cells for the first method (see Table 1 and 2 - pages 32 and 33), and total cells for the second method (see Table 3). The P-cells are calculated manually.

A sample of each receptor image is presented in Figure 3 and Figure 4 for ER and PR, respectively. Image A of all figures are original image; the second one (i.e. B) represents the image preprocessed. Image C is the output of ANN (second code) which converts color images to gray scale images, where the positive stained cells have dark regions and the negative stained cells will have less darkened regions, and the background which represents the unwanted region will have white colors. The final image (D) of each figure are also the colored image which showed P-cells (green color) and N-cells (red color). The number of both cells, proportion observation percent (PO%), and Proportion Staining (PS) is displayed above the image D. The paired statistical samples for both methods are computed by SPSS program and find non-significant evaluation for the two methods.

## Discussion

As mentioned in previous sections, some preprocess steps have been done before entering images into the first Matlab code. These steps include resize and re-dimension of all slide images because nearly all of them have large dimensions and sizes that cause a very long run and may 'freeze' the computer. The images are re-dimensioned from large dimensions (such as 2592x1944) to small dimension (like 550x413), and resized from ~1.5 MB to ~100 KB to be found suitable (small time of running) for Matlab codes. Also, some images required the removal of unwanted regions which affected the final results and will be one of the sources of errors.

Figure 2:  
Follow chart of third code



We enhanced some images to increase clarity for the two colors, Brown for positive stained cells (P-cells) and Blue for negative stained cells (N-cells). One or some of functions, from the Photoshop program, were used to obtain these results.

Most important parameters for running and obtaining parameters for all ER and PR slide images showed that the most suitable number of hidden layers was two, because the first or third layers did not give proper results. After optimization, we found that the two layers with the same number of neurons give better results than different numbers for the two layers. Also parameters were optimized like target vector (-1, 0.5, 1) and goal ( $1 \times 10^{-17}$ ) to get the best results. Best

results obtained for the range of neurons 4-13 and neglect time of running for very small epoch, and performance (i.e. mean square error) were in the range  $10^{-17}$ - $10^{-30}$ . The very small time consumed for each case is an indicator that the programmed Matlab codes have very good performance.

Some original images have noisy parts which may be related to dirty samples, processes of staining or imaging techniques. These noisy parts affected the final results in some way which have been nearly corrected. Also, clear enhancing of images was seen for some images (as shown in Figures 3 and 4). This describes the importance of using preprocessing steps before running the Matlab codes.

Manual Scoring								Computer scoring				Average of method	
No.	Name	Average P-cells	SD	Average N-cell	SD	PO% cells	PS	P-cell	N-cell	PO%	PS	Average	SD
1	Er	408.33	45.00	338.33	63.51	54.68	4	407.47	340.04	54.51	4	54.5	0.12
2	Er1	125.06	19.11	82.13	29.57	60.36	4	59.34	86.25	40.76	4	50.5	13.85
3	Er2	106.4	16.45	60.8	18.28	63.63	4	50.21	67.65	42.60	4	53.1	14.87
4	Er3	83.06	42.03	116.66	44.45	41.58	4	50.60	99.37	33.74	4	37.6	5.54
5	Er4	99.86	14.02	126	12.12	44.21	4	98.32	99.53	49.68	4	46.9	3.86
6	Er3 erpr	123.66	67.26	91	12.12	57.60	4	127.58	126.84	50.14	4	53.8	5.27
7	Er2 erpr	97.53	17.72	125.06	19.61	43.81	4	91.52	68.34	57.25	4	50.5	9.50
8	Er1 erpr	63.93	16.4	106.4	7	37.53	4	81.72	99.36	45.13	4	41.3	5.37

Table 1: Shows the results of manual and computer scoring for ER

By comparison between image B and C for all slides, one can see that the programmed Matlab ANN codes have excellent ability to distinguish P-cell and N-cells by techniques of color pixels classification for DAB staining slide images. But, in the case of AEC staining slide images, there are just classifications of colors into black and gray regions because P-cells have both colors (i.e. blue for nucleus and rose red for their cytoplasm).

For image D of all slides stained by DAB method, P- and N-cells counting, PO% and PS were obtained from the third Matlab code due to their different colors for different types of cells. But for other slides that were stained by AEC method, the third code

can count total cells only and P-cells count is done manually (so other parameters computed PO% and PS) because P-cells have both colors. So, accordingly DAB stain is better than AEC stain.

The statistical evaluation is one of non-significance between the two methods which indicates that the two methods can be used correctly with the difference that the author's method is objective and gives more accurate and reliable values.

### Conclusion

In view of the results presented in this study, one can conclude that this new program can compute efficiently: PO% for ER

Manual Scoring								Computer scoring				Average	
No.	Name	Average P-cells	STDEV	Average N-cell	STDEV	PO%	PS	P-cell	N-cell	PO%	PS	Average	STDEV
1	Prs3	19.44	0.971	33.755	4.766	36.54	4	24.317	21.44	53.14	4	44.8	11.7
2	Prs2	135.5	13.02	155.76	21.24	46.52	4	144.92	148.42	49.40	4	47.9	2.0
3	Pr3	83.53	42.00	112.93	47.62	42.51	4	86.62	78.01	52.61	4	47.5	7.1
4	Pr2	263.2	97.51	345.33	39.80	43.25	4	312.6	325.7	48.97	4	46.1	4.0
5	Pr1	115.2	33.61	74.2	17.54	60.83	4	97.91	70.95	57.98	4	59.4	2.0
6	Pr	1082	345.3	710.5	193.6	60.37	4	1117.4	287.81	79.51	5	69.9	13.5
7	Pr erpr	72.8	29.79	70	20.90	50.98	4	43.98	56.07	43.95	4	47.4	4.9

Table 2: Shows the results of manual and computer scoring for PR

and PR. The program is better than previous methods due to its objectivity (the results are not affected by conditions of the patient like excitation, fatigue) and showing PO% in a very accurate manner. Also, it's necessary to resize and re-dimension (if the images have sizes >100 kB and dimensions larger than 550x550) to prevent a long running period or consequently often freezing the computer (these values are altered according to the efficiency of the computers). Removal of noisy parts and enhancing of images must be done to obtain better results.

Finally, staining of slides by DAB methods gave best results because positive and negative cells colored differently. But in the case of AEC methods the results were not good (just computing total cells) due to different colors of nucleus and membrane of the same cells.

### References

- Bernoux A., Cremoux P., Laine-Bidron C., Martin E., Asselain B., and Magdelenat H., (1998), "Estrogen receptor negative and progesterone receptor positive primary breast cancer: pathological characteristics and clinical outcome", *Breast cancer research and treatment*, 49: 219-225.
- Gown A., (2008), "Current issues in ER and HER2 testing by IHC in breast cancer", *Modern Pathology*, 21, S8-S15.
- Hakan O., (2000), 'Estrogen Receptor Content in Malignant Breast Tumors in Men- a Review', *Journal of Mammary Gland Biology and Neoplasia*, Vol. 5, No. 3.
- Huang A., Leygue E., Dotzlaw H., Murphy L., and Watson P., (1999), "Influence of estrogen receptor variants on the determination of ER status in human breast cancer", *Breast*

Manual Scoring								Computer scoring				Average	
No.	Name	Average Total-cells	STDEV	Average P-cells	STDEV	PO%	PS	Total-cell	P-cell	PO%	PS	Average	STDEV
1	Pr401	49	3.46	28.667	2.081	58.50	4	41	28.66	69.90	5	64.2	8.0
2	Pr301	117.3	7.63	48.33	2.081	41.19	4	102	47.385	46.45	4	43.8	3.7
3	Pr201	121.3	6.65	57.66	8.386	47.52	4	104	57.666	55.44	4	51.4	5.6
4	Pr101	99.33	5.50	27.667	2.886	27.85	3	114	27.667	24.26	3	26.0	2.5

Table 3: Shows the results of manual and computer scoring for PR

Cancer Research and Treatment, 58: 219-225.

Khoshnoud M., (2008), "Long-term pattern of disease recurrence among patients with early-stage breast cancer according to estrogen receptor status and use of adjuvant tamoxifen", *Breast Cancer Res Treat*, 107:71-78.

Krecsák L., Micsik T., Kiszler G., Krenács T., Szabó D., Jónás V., Császár G., Czuni L., Gurzó P., Ficsor L., and Molnár B., (2011), "Technical note on the validation of a semi-automated image analysis software application for estrogen and progesterone receptor detection in breast cancer", *Diagnostic Pathology*, 6:6.

Liu S., Chia S., Mehl E., Leung S., Rajput A., Cheang M., and Nielsen T., (2010), "Progesterone receptor is a significant factor associated with clinical outcomes and effect of adjuvant tamoxifen therapy in breast cancer patients", *Breast Cancer Res. Treat.*, 119:53-61.

Mansel R., Fodstad O., and Jiang W., (2007), "Metastasis of Breast Cancer", 1st edition, Springer pub., Netherlands.

Patil A., Bhamre R., Singhai R., Tayade M., and Patil V., (2011), "Estrogen receptor (ER) and progesterone receptor (PgR) in breast cancer of Indian women", *Breast Cancer: Targets and Therapy*, 3, 27-33.

Sertel O., (2010), "Image Analysis For Computer-Aided Histopathology", PHD dissertation, Ohio State University.

Siganos D., (2011), "Neural Networks in Medicine", address: [http://www.doc.ic.ac.uk/~nd/surprise\\_96/journal/vol2/ds12/article2.html](http://www.doc.ic.ac.uk/~nd/surprise_96/journal/vol2/ds12/article2.html), accessed at 4-10-2011.

Smith B., (2006), "Nanoparticulate Platforms for Molecular Imaging of Atherosclerosis and Breast Cancer", PHD Dissertation, Ohio State University.

Thiran J., and Macq B., (1996), "Morphological feature extraction for the classification of digital images of cancerous tissues", *IEEE Transaction on biomedical engineering*, Vol. 43, No. 10.

Yu K., Di G., Wu J., Lu J., Shen k., Liu G., Shen Z., and Shao Z., (2008), "Breast cancer patients with estrogen receptor-negative/progesterone receptor-positive tumors: being younger and getting less benefit from adjuvant tamoxifen treatment", *J Cancer Res. Clin. Oncol.*, 134:1347-1354.

Zhu H., (2003), "Medical Image Processing Overview", University of Calgary, Summer School Program - Introduction to Mathematical Medicine, held at the University of Waterloo.

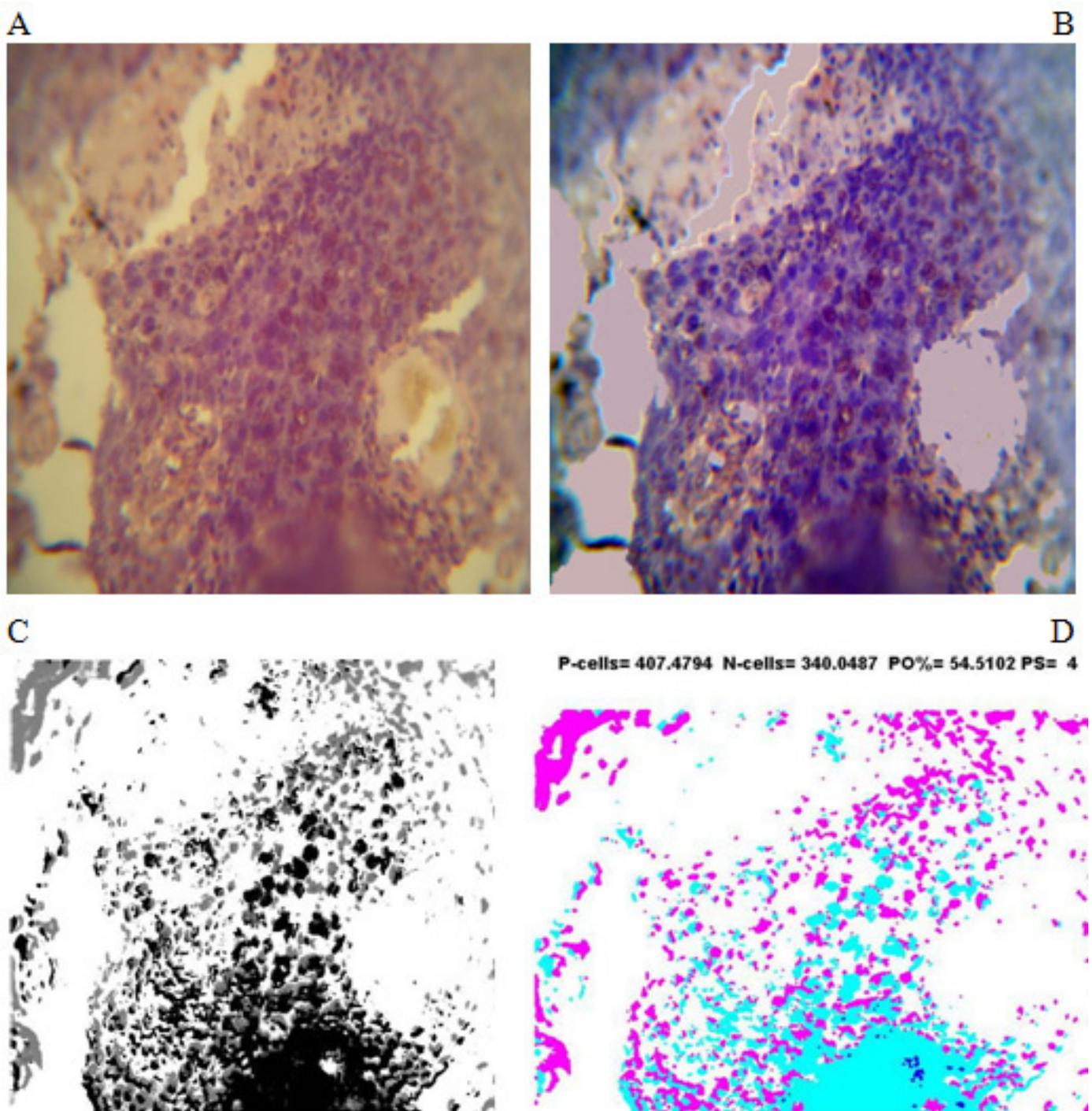


Figure 3: Shows the final results from the Matlab codes for image Er (A: original image(400x), B: preprocess steps (applied Auto Tone command), C: image output of ANN (black color for P-cells, gray color for N-cells), D: colored image with total count of P-cells (Green color), total count of N-cells (Red color) (Proportion observation percent (PO%), and Proportion staining (PS) displayed on the top of the image)

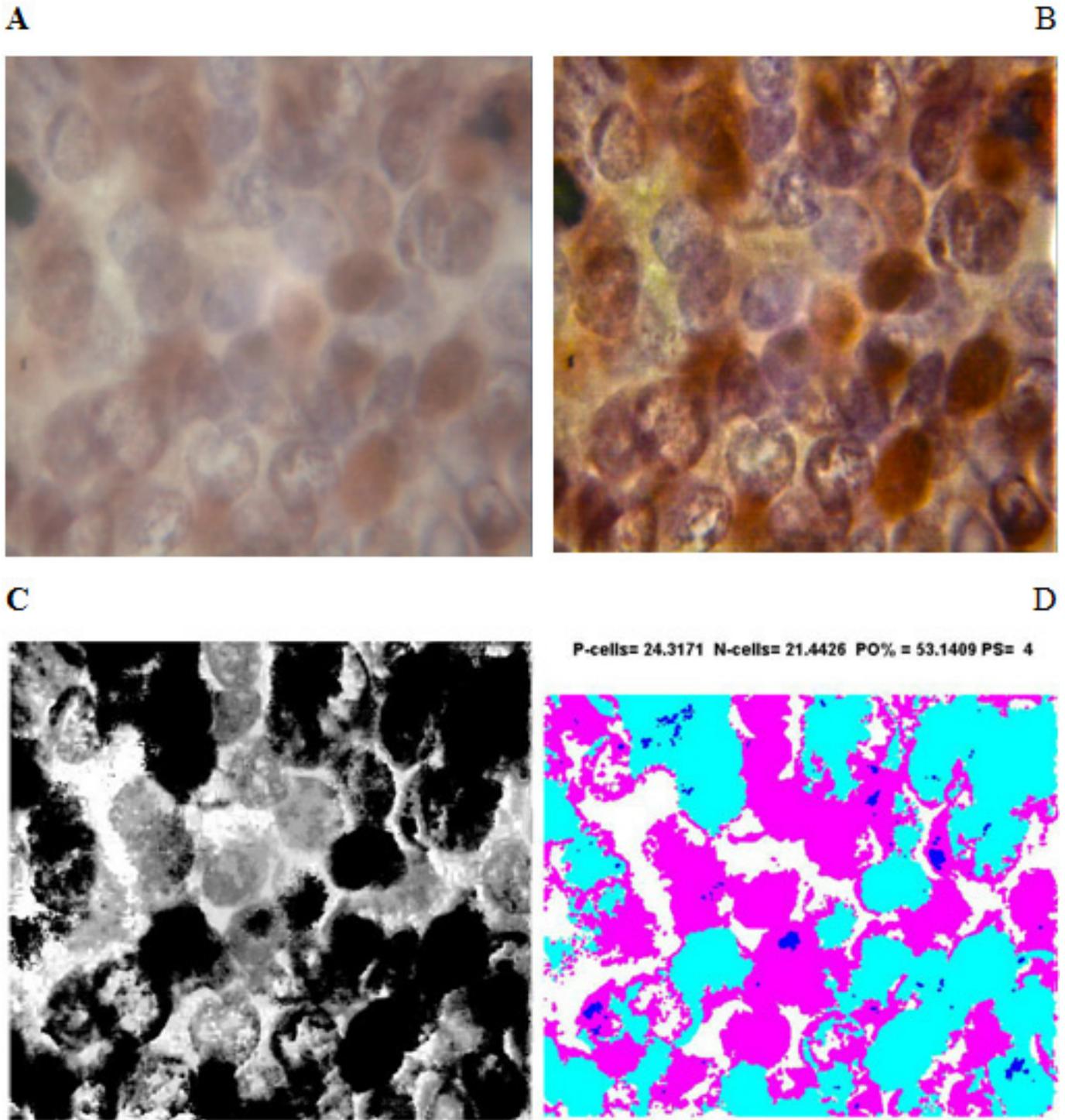


Figure 4: Shows the final results of the Matlab codes for image Pr (A: original image (1000x), B: preprocess steps (HDR Toning command), C: image output of ANN (black color for P-cells, gray color for N-cells), D: colored image with total count of P-cells (Green color), total count of N-cells (Red color), Proportion observation percent (PO%) and Proportion Staining (PS) displayed on the top of the image)

# The role of Magnetic Resonance Imaging in diagnosing common disorders of the knee. Our experience at King Hussein Medical Centre

## ABSTRACT

**Objectives:** The aim of our study was to evaluate Magnetic Resonance Imaging appearances in various conditions affecting the Knee joint, and to calculate the percentages of abnormal findings compared to total studies performed during fourteen months at Radiology department in King Hussein Medical Centre.

**Methods:** During the period October 2010 - January 2012, a total number of 308 patients (238 males and 70 females), aged 11-52 years old, presented with common symptoms of knee pain at King Hussein Medical Centre and on whom we performed Knee MRI to exclude meniscus or ligament injury of the knee, were retrospectively reviewed. Old age groups with degenerative bony or articular processes were excluded from this study. According to clinical follow up, arthroscopic findings and post operative results, the normal, abnormal MRI diagnosis and type of abnormality were recorded.

**Results:** Out of 308 patients on whom we performed MRI for possible knee joint pathology findings, in 179 patients (58.1%) the examination was positive and in 129 patients (41.9%) the examination was normal. The most common abnormality found was tear in the posterior horn of medial meniscus (75 patients) and accounted for 24.4% of total patients examined and represented 41.9% of total abnormalities. The least common abnormality was found in patients with bone infarct, medial collateral ligament tear, meniscus cyst and osteochondritis dissecans, all these represented by one patient. .

**Conclusion:** We conclude that MRI is sufficiently accurate in diagnosing common disorders of the knee, with preservation of knee arthroscopy for therapeutic tools preceded by MRI assessment.

**Key words:** MRI, Knee disorders

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### Introduction

One of the most common presenting features in musculoskeletal pathology to the radiologist is knee pain, and most symptoms are due to acute knee injury or due to gradual increase in patients symptoms(1). MRI is believed to be the modality of choice for most orthopaedic surgeons in detecting intra articular knee pathology due to many advantages especially in diagnosing ligament or meniscal injury(2). MRI is superior to other diagnostic procedures due to lack of ionizing radiation, safety and it has the ability to assess the internal structures in multiple planes (2,3). The accuracy in detecting ligament or meniscal injury by MRI is now considered to be 93% or more(2,14). Plain X-ray films are widely used in detecting common bony or joint abnormality such as osteoarthritic changes, joint space narrowing, subchondral cysts and sclerotic borders of the joints(19), but these changes are commonly found in elderly patients. Arthroscopy of the knee joint represents the gold standard for diagnosing internal knee pathology and playing an essential role in managing these abnormalities, but it is well known that patient admission and anesthesia should be considered in this uncomfortable and invasive technique for every patient (4,6,11). In addition the arthroscopic procedure carries accuracy of 95% in diagnosing common disorders of the knee (7).

### Methods

This is a retrospective review of 308 patients who presented with chief complaints of knee pain and on whom we performed MRI to exclude intra articular knee pathology at King Hussein Medical centre (KHMC) during 14 months between October 2010 - January 2012. There were 238 males and 70 females with M:F Ratio of 2.4:1. All patients selected for this study were of young and middle age groups (between 11-52 years) with mean age of 32.3 years. Old age groups with degenerative bony or articular processes were excluded from this study. Two MRI Machines (1.5 T symphony Siemens and

Abnormal findings	No. of patients
Medial meniscus tear	75
Lateral meniscus tear	4
ACL rupture	38
Baker's cyst	15
PCL tear	3
MCL(Medial collateral) tear	1
Stress fracture	3
Enchondroma	11
Knee effusion	19
Loose bodies	4
Chondromalacia patellae	6
Synovial plicae	3
Bone cyst	2
Ossifying fibroma	2
Bone contusion	9
Discoid lateral meniscus	3
Meniscal cyst	1
Tumors	4
Osteomyelitis	1
Osteochondral defect	4
Osteochondritis dissecans	1
Bone infarction	1
Two or more abnormalities	33
Normal MRI exam.	129

Trio 3T Siemens) were used. Axial fat saturated, coronal T1 W Images and sagittal T1 and T2W images were taken for every patient. We retrospectively reviewed all requests and radiological reports for this group of patients and based on clinical follow up, arthroscopic findings and postoperative results, we made our calculations and conclusions.

## Results

Table 1 summarizes the frequency of each pathological type of intra articular knee joint pathology, of which posterior horn of medial meniscus was the most common injury detected (Figure 1) and was reported in 75 patients (41.9%) of all abnormalities, followed by anterior cruciate ligament injury (Figure 2) reported in 38 patients (21.2% of total positive findings. The lateral meniscus tear was seen in only four patients (2.2%), whereas posterior cruciate (PCL) injury was reported in only 3 patients (1.7%)(Figure 3). Backer's cyst was found in 15 patients and knee joint effusion in 19 patients. Only in one patient we revealed Medial Collateral Ligament (MCL) injury, bone infarction, meniscal cyst and osteochondritis dissecans. Tumours were found in 4 patients and according to Histopathological results, they were malignant in 2 patients, one of them in the extra articular soft tissue region (Figure 6) and benign in the other two patients. Two or more pathologies in same patient were found in a sum of 33 patients.

Table 1: Frequency of each type of knee pathology in the study



Figure 1: Sagittal T1 Proton density (a) sagittal STIR (b) and coronal gradient (c) sequences showing oblique tear in posterior horn of medial meniscus reaching articular surface in a 34 years old male patient who presented with history of twisting knee injury (arrows)

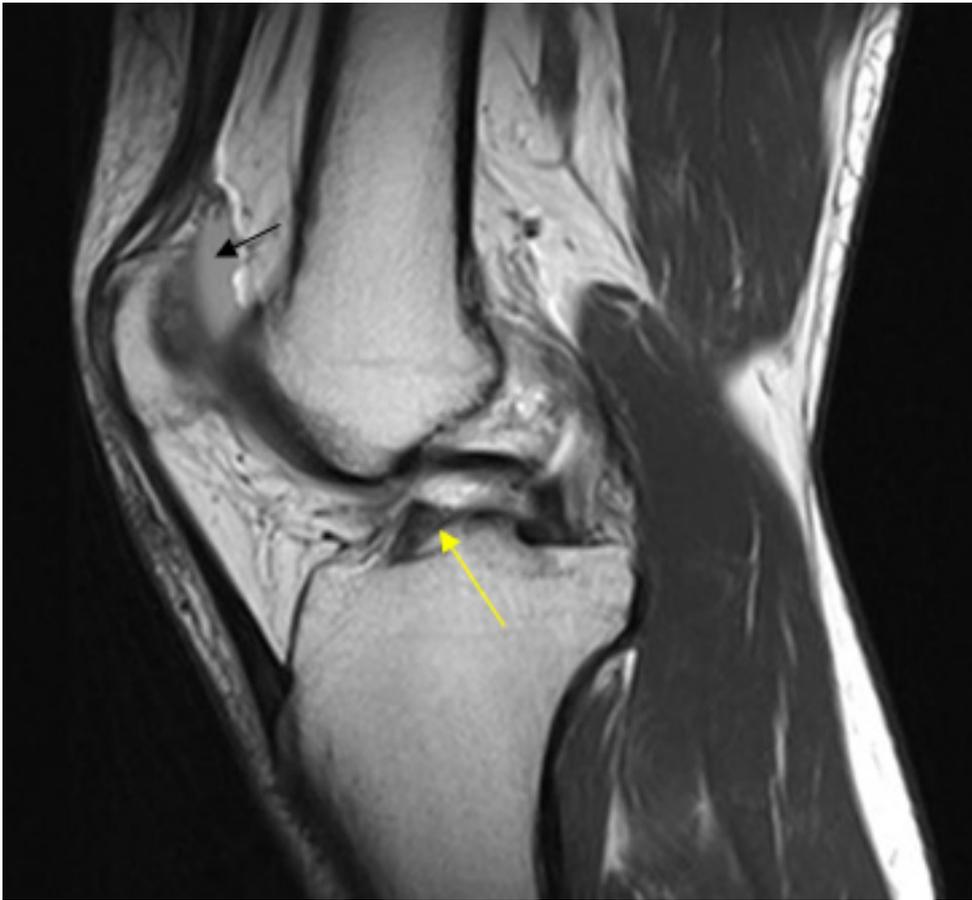


Figure 2: sagittal T2WI shows full thickness tear of anterior cruciate ligament (yellow arrow), along with buckling of posterior cruciate ligament as an indirect sign, note the associated knee joint effusion (black arrow)

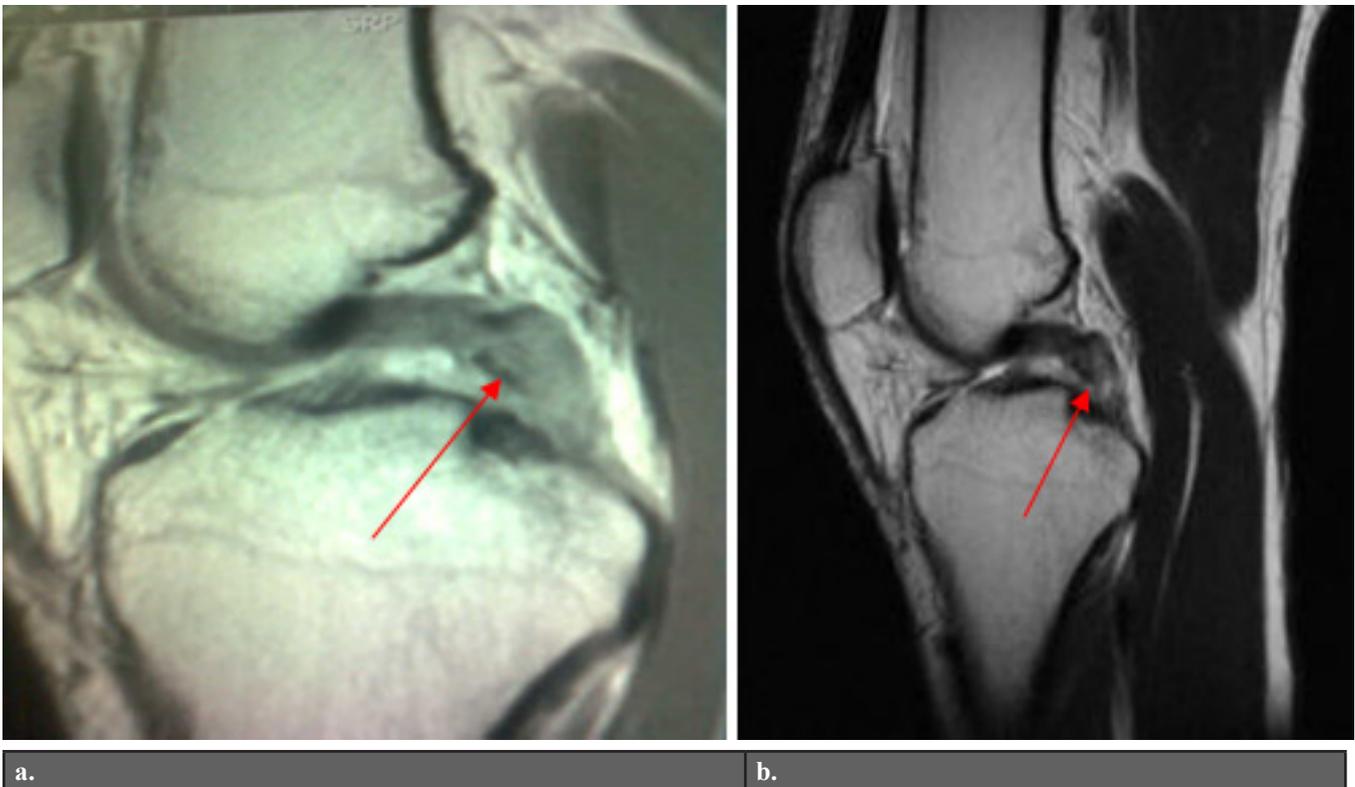


Figure 3: sagittal T1WI (a) and sagittal T2WI(b) shows significant thickening and high signal intensity in the posterior part of posterior cruciate ligament indicating acute PCL injury, in a 28 years old male patient (arrows)



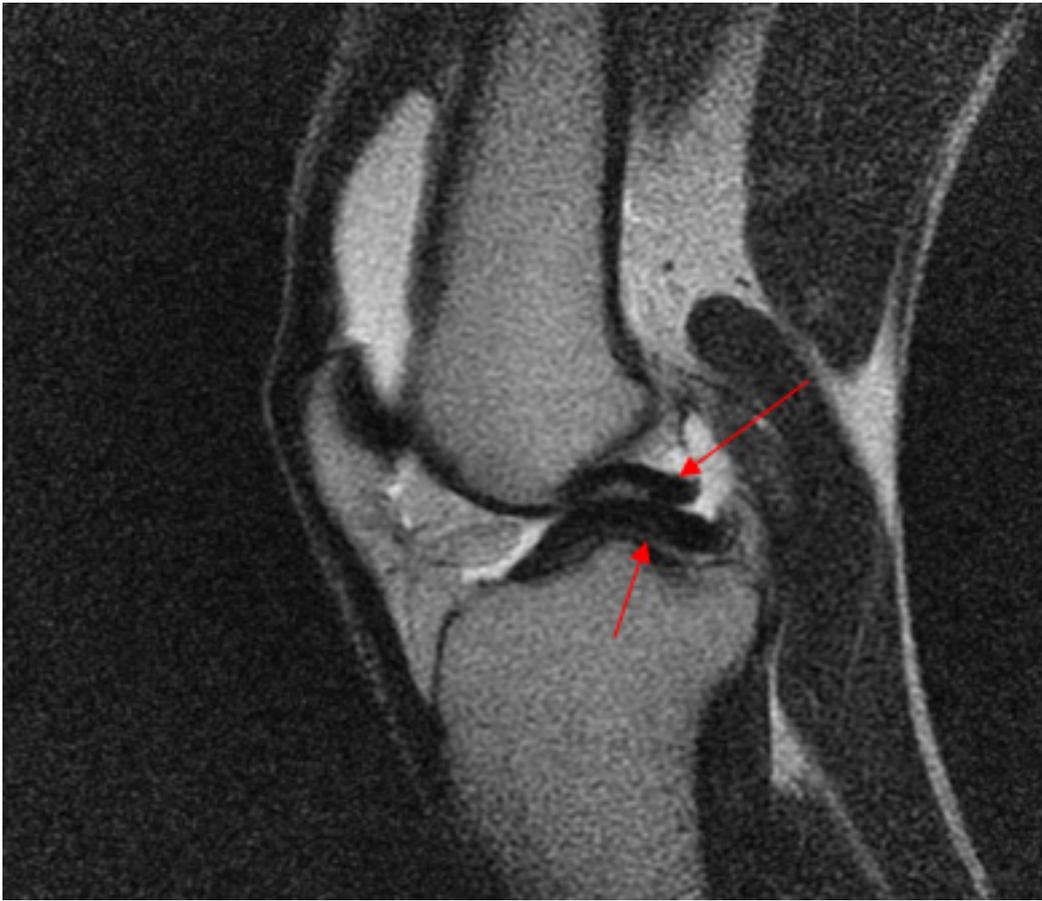
Figure 4: Gradient sagittal showing well defined oval shaped bone intensity lesion (arrow) representing loose body



Figure 5: Gradient sagittal shows fluid intensity Anterior Cruciate Ligament cyst



Figure 6: soft tissue sarcoma in the posterior aspect of the lower thigh in a 20 years old female patient (arrow)



**Figure 7: Bucket handle tear, Double posterior cruciate (PCL) sign**

## Discussion

Plain X-ray films are still used as first diagnostic step in evaluating knee pathology, but they lack information about many pathological conditions. They can diagnose bony fractures, osteoarthritic changes, knee effusions and joint space narrowings. In many studies the abnormal findings on simple plain X-ray do not exceed 7% of all exposures performed for suspected knee pathology(10,13). Torg et al , Jonsson et al , Donaldson et al , Zarins& Rowe commonly used Lachman clinical test and recorded high accuracy in detecting acute and chronic anterior cruciate ligament (ACL) injury with less sensitivity for other pathology involving the knee joint, not reaching 100% in some experienced hands and this is preserved for ACL injury(5,16). An arthrography is still used in many centers in order to support the diagnosis but has the disadvantages of using ionizing radiation and can be uncomfortable for the patient(7,17). Despite the accuracy of arthroscopy being considered very high in diagnosing meniscal and ligamentous injuries of the knee and exceeding 95%(7,17), there are many disadvantages and complications of the procedure including exposure to ionizing radiation, anesthesia, admission of the patient and possible secondary infections and not uncommonly complicated by postoperative bleeding, persistent swelling, neurovascular injury, and pulmonary embolism(17,20,21). Meniscal injury of the knee among young age groups is considered to be more evident due to acute trauma, whereas in the older age group as degenerative cause for meniscal tears is more common(9). MRI was introduced in clinical practice in the mid 1980s with establishment of its role in the last two decades for diagnosing internal derangements of the knee joint(15). It is trusted to be highly accurate in detecting meniscal and

ligamentous injury of the knee (4,9,12,15). MRI combination with vigorous clinical examination represents an effective tool in selection of patients for therapeutic arthroscopy and avoiding unnecessary surgery(14,15,18). In our sample the posterior horn of medial meniscus was the most commonly reported injury and was found in 49.1% of total abnormalities. Metcalf et al reported the patterns of posterior horn of medial meniscus tear as oblique or vertical longitudinal in 81% of cases and can be complete or incomplete and commonly associated with ACL injury(2,9,22). Posterior cruciate ligament is seen less commonly than other types of ligamentous injury of the knee(8). The frequency of each type of intra articular knee pathology diagnosed by MRI in our study has been correlated well with recent studies being made for this scope. By correlation of MRI reports and compared with clinical, arthroscopic and surgical follow up we found that MRI accuracy was about 88.4% in our study, whereas arthroscopic sensitivity in recent studies ranges from 90% to 95% in diagnosing internal knee joint pathology.

## Conclusion

We conclude that MRI is sufficiently accurate in diagnosing common disorders of the knee, with preservation of knee arthroscopy for therapeutic tools preceded by MRI assessment.

## References

1. S Ostlere, Imaging the knee. Nuffield Orthopaedic Centre and Oxford Radcliffe Hospital, Oxford, UK. Imaging, volume 15(2003),217-241. The British institute of Radiology .

2. Patrick E. Greis, Davide D. Bardana, Michael C. Holmstrom, Robert T. Burks Meniscal injury: Basic Science and evaluation. *J Am Acad orthop surg* 2002.10.168-176
3. Monica Koplak et al. The painful knee: choosing the right imaging test *Cleveland Clinic Journal Of Medicine*. Volume 75. Number 5 May 2008
4. Gul-e-khanda, Wseem Akhtar, Humera Ahsan, Nadeem Ahmad. Assessment of Menisci and ligamentous Injuries of the Knee on Magnetic Resonance Imaging: Correlation with Arthroscopy. *J Pak. Med. Assoc.* Vol. 58, No. 10, Oct. 2008
5. Stephen H. Liu, Leonard Costi, Mark Henry, Luigi Bocchi. The diagnosis of acute complete tears of the anterior cruciate ligament. *The journal of bone and joint surgery*, Vol. 77-B, No. 4, July 1995.
6. Asif Rahman, Muhammad Nafees, Muhammad Hamid Akram, Atif Hussain Andrabi, Muhammad Zahid. Diagnostic accuracy of Magnetic Resonance Imaging in meniscal injuries of the knee joint and its role in selection of patients for arthroscopy.
7. S.P Fischer, J.M. Fox, Del Pizzo, M.J. Friedman, S.J. Synder, R.D. Ferkel. Accuracy of Diagnoses from Magnetic Resonance Imaging of the Knee. *The journal of bone and joint surgery*. Vol. 73-A, No. 1, January 1991 .
8. David R. McAllister, Frank A. Petrigliano. Diagnosis and Treatment of Posterior Cruciate Ligament Injuries. *Current Sports Medicine Reports* 2007, 6: 293-299. Current medic group LLC ISSN 153-890x .
9. Nicola Maffulli, Umile Giuseppe, Stefano Campi, Vincenzo Denaro. Meniscal tears. *Open access journal of sports medicine* 2010; 1, 45-54.
10. Ian G. Stiel et al. Implementation of the Ottawa Knee Rule for the Use of Radiography in Acute Knee Injuries. *JAMA*, December 17, 1997-Vol. 278, No. 23.
11. Vassilios S Nikolaou, Efstathios Chronopoulos, Christ ianna Savvidou, Spyros Plessas, Peter Giannoudis, Nicolas Efstathopoulos & Georgios Papachristou. MRI efficacy in diagnosing internal lesions of the knee: a retrospective analysis. *Journal of trauma Management & outcome* 2008, 2: 4 doi:10.1186/1752-2897-2-4.
12. Ruth Crawford, Gayle Walley, Stephen Bridgman, Nicola Maffulli. Magnetic Resonance Imaging versus arthroscopy in the diagnosis of knee pathology, concentrating on meniscal lesions and ACL tears : a systematic review. *BRITISH Medical Bulletin* 2007, 84-5-23. DOI:10.1093/bmb/dm022.
13. Jeffrey L. Jackson, Patrick G. O'Malley, Kurt Kroenke. Evaluation of Acute Knee Pain in Primary Care. *Ann Intern Med.* 2003; 139:575-588, Vol. 139. No. 7
14. Vincken et al. Effectiveness of MR Imaging in selection of patients for Arthroscopy of the knee. *Radiology* 2002 ; 223: 739-746
15. Edwin H.G Oei, Jeroen C.M Verstijnen, Abida Z. Ginai, M.G. Myriam Hunink. MR Imaging of the Menisci and Cruciate Ligaments: A Systemic Review. *Radiology* 2003 ; 226: 837-848.
16. TR Madhusudhan, TM Kumar, SS Bastawrous, A Sinha. Clinical examination, MRI and arthroscopy in meniscal and ligamentous knee injuries - a prospective study. *Journal of Orthopedic surgery and Research* 2008 , 3: 19 doi:10.1186/1749-799X-3-19
17. N.R Boeree, A.F. Watkinson, C.E. Ackroyd, C. Johnson. Magnetic Resonance Imaging of meniscal and cruciate injuries of the knee. *The journal of bone and joint surgery*. *J Bone Joint Surg (Br)* 1991; 73-B: 452-7.
18. Matthew Hoyt, DO, Patricia Goodemote, Jackie Morton, MLS. How accurate is an MRI at diagnosing injured knee ligaments? *The journal of family practice* Feb. 2010 Vol. 59. No 2
19. D. Lee Bennett et al. American College of Radiology (ACR) Appropriateness Criteria Nontraumatic Knee Pain. 1995, review 2008.
20. Gert Scsippinger et al. Thromboembolic complications after arthroscopic knee surgery. Incidence and risk factors in 101 patients. *Acta Orthop Scand* 1998; 69(2): 144-146.
21. Orrin H. Sherman & James M. Fox et al. Arthroscopy- No Problem Surgery. An analysis of complications in two thousands and six hundred and forty cases. *The journal of Bone and Joint Surgery* . Vol. 68-A, NO. 2, February 1986
22. Metcalf RW, Burks RT, Metcalf MS, McGinty JB. Arthroscopic meniscectomy. In: McGinty JB, Caspari RB, Jackson RW, Poehling GG, eds. *Operative arthroscopy*. Second edition. Philadelphia: Lippincott-Raven Publishers, 1996: 263-97.

# Sub-Cutaneous Emphysema and Pneumo-Mediastinum in the Perioperative Period

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## ABSTRACT

Sub-cutaneous emphysema and pneumo-mediastinum may occur as a rare complication during or immediately after surgery. It can be caused by tracheal intubation related airway or esophageal ruptures. A case of sub-cutaneous emphysema and pneumomediastinum during the perioperative period is reported. The patient was observed with sub-cutaneous emphysema of face and chest wall within a few minutes after surgery. HRCT revealed sub-cutaneous emphysema and pneumo-mediastinum.

**Key words:** sub-cutaneous emphysema, pneumo-mediastinum, endotracheal intubation, Perioperative period.

### Key Message:

Surgical emphysema and pneumomediastinum are a very rare complication of endotracheal intubations and peri-operative retching. The diagnosis is confirmed by CT scan after strong clinical suspicion. The present report highlights the importance of a high index of clinical suspicion and timely utilization of CT scan while routine investigations miss the diagnosis.

## Introduction

Sub-cutaneous emphysema occurs when air gets into tissues under the skin. Air in the mediastinal tissue is referred to as Pneumo-mediastinum or mediastinal emphysema. They may occur spontaneously or after trauma (iatrogenic/non-iatrogenic). Sub-cutaneous emphysema and pneumomediastinum resulting from anesthetic procedures or from vomiting are very rarely reported.

## Case Report

A 10 year old child underwent an uneventful right herniorrhaphy repair (Bassinis) for indirect inguinal hernia.

Her past medical history was not significant.

General anesthesia was induced. The patient was intubated using Mc Intosh laryngoscope with 2" number blade and a 5.5" endotracheal tube on first attempt without difficulty or evident trauma. Induction was done with inj. thiopental sodium 150mg dil. in 10cc with atropine 0.6mg i.v. Anesthesia was maintained using succinylcholine 50mg i.v. vecuronium 3 mg stat. followed by 0.6mg twice in ½ hour intervals. At the end of surgery, the neuromuscular blockade was reversed, the patient was awakened, and extubated. Ondansetran injection 4 mg i.v was administered for nausea.

Ten minutes after arriving in the post-operative ward, the patient experienced an episode of nausea, retching and vomited a small amount (about 15-20ml) of clotted blood with gastric contents within 10 minutes of this event. Duty doctors noticed swelling over the left half of her face and the periorbital area. Complete examination revealed swelling and crepitus involving the left half of her face, the entire anterior part of her neck, and the entire left half of her chest extending down to the upper abdomen. On the right side of the chest the emphysema extended up to her nipples only. No dyspnoea, oxygen desaturation or hemodynamic instability was noted at that time. On auscultation, surgical crepitus was felt and heard and normal breath sounds were heard throughout the chest. Hamman's sign was negative. E.C.G. was normal. A portable radiography showed pneumo-mediastinum and bilateral sub-cutaneous emphysema of the neck and chest wall. There was no evidence of pneumothorax.

She was kept under continuous observation in RICU to watch for sudden airway compromise and related complications. Patient was administered high flow oxygen; further observation did not show any airway compromise. A baseline HRCT was done which showed sub-cutaneous emphysema with pneumo-mediastinum. (Figures 1 and 2 - next page),

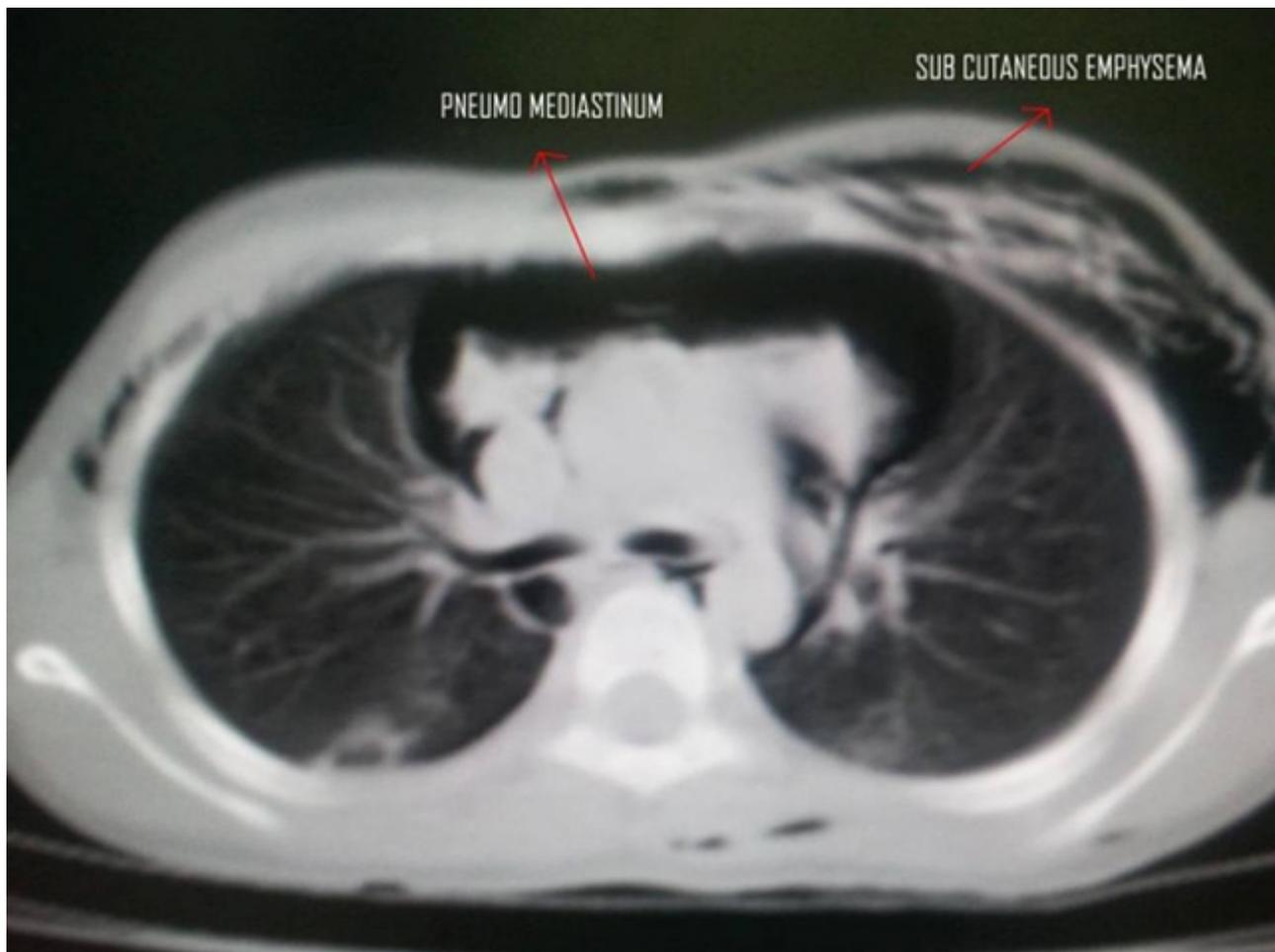


Figure 1

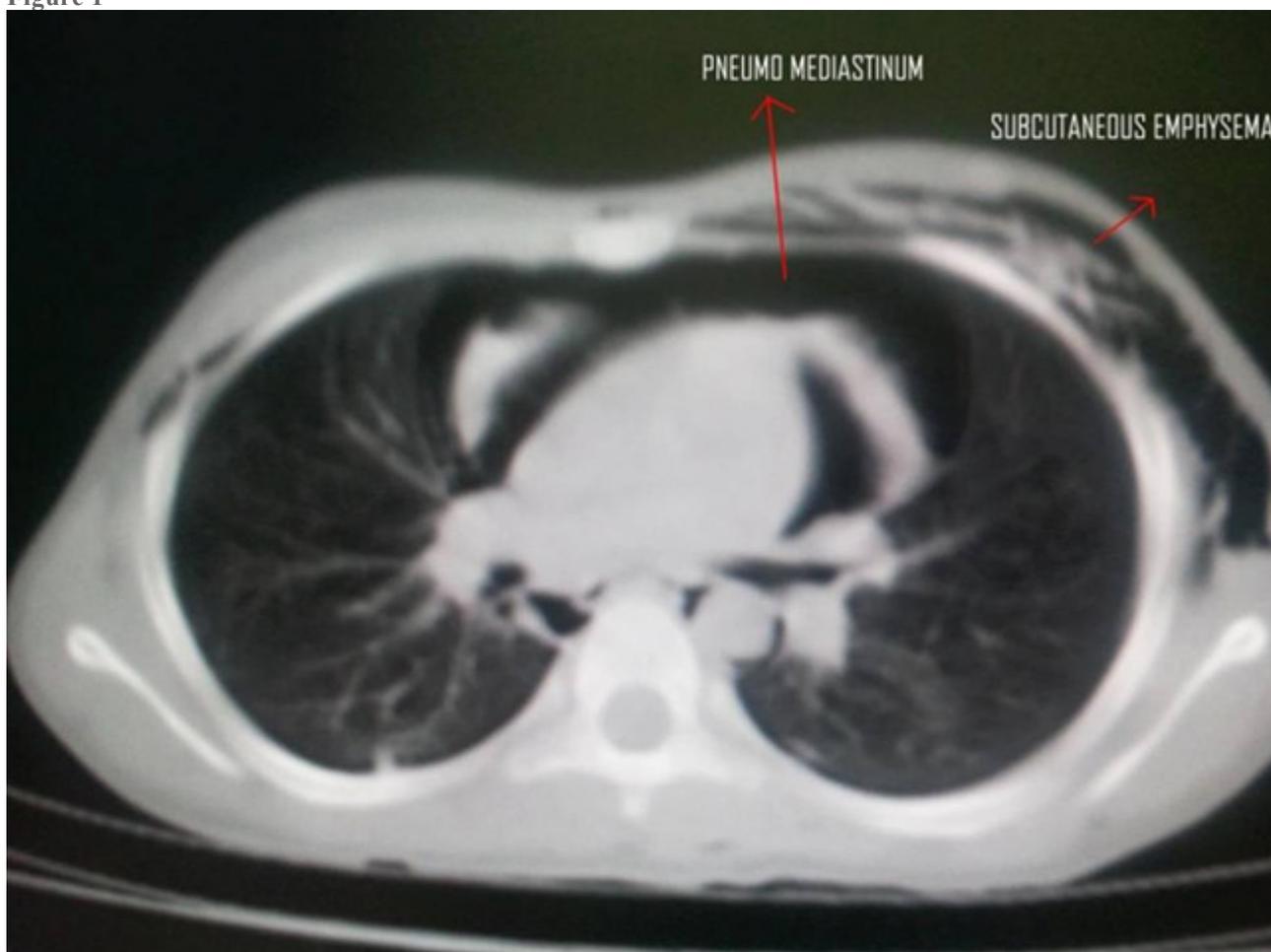


Figure 2

An opinion from the cardiologist, pulmonologist and ENT specialist opinion were sought. A fiberoptic bronchoscopy was planned but was refused by patient's family members.

Patient was observed in the RICU for 4 days, there was gradual resolution of the sub-cutaneous emphysema. Patient recovered without any complications.

## Discussion

This report describes rapidly progressive sub-cutaneous emphysema and pneumomediastinum during the perioperative period. Differential diagnosis includes alveolar rupture, hypo pharyngeal perforation, tracheobronchial lacerations and Boerhaave syndrome.(1, 3) In order to establish the correct diagnosis, imaging studies and bronchoscopy must be performed promptly.(3)

Increased alveolar pressure produced by Valsalva maneuver (vomiting) may cause alveolar rupture and result in sub-cutaneous emphysema and pneumomediastinum. These cases are notable for their lack of sequelae and their spontaneous resolution.(1)

Trauma to pharynx, esophagus or trachea from laryngoscopy, intubation, and cuff inflation is one potential explanation. In our patient there was no indication that any of these procedures were difficult or caused trauma, although there is a possibility of occult injury.

Bronchoscopy is helpful in visualizing the tear in some patients, but our patient was in a state of apprehension and had refused any further invasive procedures.

Mechanical factors such as vigorous attempt of intubation, inexperienced anesthesiologist, over-inflation, rapid inflation, rupture of cuff, patient movement with bronchial cuff inflated, inadequate tube size, use of stylet and vigorous coughing contribute to tracheal rupture.

Possible anatomical factors such as congenital tracheal abnormalities, chronic obstructive pulmonary disease, and inflammatory lesion of the tracheobronchial tree, steroid therapy, lymph nodes or neoplasm causing distortion of the trachea can predispose to tracheal rupture.

Almost all cases of post intubation tracheal lacerations are reported in short females. Our patient also was short (height 133 cm). The diagnosis is suspected at extubation or 2-6 hours later. The laceration usually occurs longitudinally in the posterior membranous wall of the trachea or at the junction of the membranous wall and the cartilaginous ring. Most injuries occur in the lower one third of the trachea. Mucosal erosion or perforation of the anterior cartilaginous tracheal wall by the tip of the tube or the stylet is very rare. (2, 3, 4)

Boerhaave syndrome presents with a classical triad of vomiting, followed by severe chest pain and rigidity of upper abdomen. All of these symptoms are not present in many cases. Early diagnosis and aggressive surgical treatment can reduce mortality and morbidity. Yet, there are several

reports of successful conservative management, when leakage is minimal or has aborted. Usually the lower esophagus is involved, with a vertical split. The irritant infective fluids and gaseous contents may be released into left pleural space. The diagnosis is confirmed by conventional contrast study or CECT. Progression to circulatory failure and death from septic shock, Pneumonitis and mediastinitis can occur.(5)

Small esophageal tears present with insidious onset and can be managed conservatively.

Patients with pneumo-mediastinum develop substernal chest pain often pleuritic, dyspnoea, dysphonia, dysphagia, odynophagia, high pitched nasal tone, either separately or in combination. Hamman's sign can be demonstrated on auscultation. E.C.G changes are low voltage, non-specific axis deviation, ST-wave changes. Chest radiography usually demonstrates a thin radiolucent strip along the mediastinal facial plane, most commonly along the left heart border. The aortic knob may be highlighted as well. CT scan chest is more sensitive for the diagnosis of pneumo-mediastinum.(6)

Conservative management may be appropriate for uncomplicated longitudinal lacerations that are < 3 - 4 cm in size, and involve less than one third of tracheal circumference. The goal is to establish airway patency for uneventful healing of injury and prevent complications.

Management includes broad-spectrum antibiotic prophylaxis, cough suppressants, extubation if feasible, mechanical ventilation to maintain low pressures, avoidance of frequent endotracheal suction, bronchoscopy for pulmonary toilet. In all published cases of conservative management, healing was uneventful, without any residual airway stenosis.

Prompt surgical repair is indicated in cases with clinical deterioration, mediastinitis or increased mediastinal fluid collection and uncontrolled air leaks. Tracheal laceration involving the cartilaginous wall always requires a surgical repair. The surgical approach is determined by the site of the injury; right thoracotomy incision for the lower third, and cervical incision for the upper two thirds of the trachea. Acute complications include tension pneumothorax, anoxia and arrhythmias. Sub-acute complications include lethal mediastinitis, pneumonitis and tracheal strictures.

In conclusion, sub-cutaneous emphysema and pneumo-mediastinum can have variegated causes like endotracheal intubation related airway ruptures or Boerhaave syndrome. A high index of suspicion is required as prompt diagnosis and early management can be life saving.

## Acknowledgement

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## References

1. Roman Schuman, David Polaner (1998) Massive sub - cutaneous emphysema and sudden airway compromise after post-operative vomiting. *Anaesth.Analg* 1999, 89:796-7
2. Charles-Henry Marty-Ane, Eric Picard, Oliver Jonquet et al (1995) membranous tracheal rupture after endotracheal intubation, *Ann. Thoracic Surgery*1995: 60:1367-1371
3. Bassam Hashem, James K Smith and W Bruce Davies (2005) A 63yrs old woman with sub-cutaneous emphysema following endotracheal intubation. *Chest* 2005 Vol.128, p1434-438.
4. David Aorte, James E Cousar , Bruce M Yergin (1979) Tracheal laceration with massive sub cutaneous emphysema ,a rare complication of endotracheal intubation .*Thorax*, 1979,34,665-669.
5. John Bancewicz, The Esophagus, Bailey and Love's Short Practice of Surgery; 24th Ed. London, Hodder Arnold, 2004, p996.
6. Cameron D. Wright, Fishman's Text Book of Pulmonary Diseases and Disorders, 4th Ed., New York, Mc Graw Hill, and p1558.

# Assessment of the Educational Environment at Tikrit University College of Medicine (TUCOM)

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## ABSTRACT

**Background:** TUCOM was established in 1989 and since its establishment adopted an innovative curriculum. There is a need to study and evaluate the educational environment in the college.

**Objective:** To measure students' perceptions of the educational environment of the TUCOM curriculum and to evaluate the internal consistency of the 50-item Dundee Ready Education Environment Measure (DREEM) Arabic version questionnaire.

**Methods:** The DREEM Arabic version questionnaire was administered to undergraduate medical students in years 2 and 3. Internal consistency of the instrument and its subscales were measured with the method described by Cronbach, and the results were expressed with alpha coefficient ranging from 0 to 1.

**Results:** The 50-item DREEM Arabic version was found highly reliable with alpha coefficient of 0.91. Scores for 10 out of 50 items (20%) were below 2, indicating areas of weaknesses of the TUCOM. Items 17, 3, 50, 23, and 33 had the lowest mean scores of the 50 items. The values for the majority of the items (96%) fell into the range that indicated aspects of the environment that would benefit from improvement (mean scores between 2 and 3). The subscale with the highest mean score was 'Academic Self-Perception' which indicates student's perception of their academic achievements. Mean score of this subscale was  $20.23 \pm 4.8$  corresponding to 63.22% of the maximum score for this domain.

The subscale with the highest mean score was students' perceptions of their academic skills:  $20.23 \pm 4.8$  out of 32, corresponding to 63.22% of the maximum score. The lowest mean score was for the students' perceptions of the college atmosphere:  $23.97 \pm 7.6$  (49.94% of the maximum score). Scores observed for year 3 students were lower in subscales SPL, SPT, and SASP compared to year 2, but the difference was not statistically significant. The overall mean score for the 50 items was  $113.91 \pm 22.46$  (56.96%).

**Conclusion:** The DREEM is a reliable and practical tool for assessing the educational environment in Iraqi Medical Colleges. The learning environment of TUCOM is perceived positively and our students' perspectives compare favorably with studies internationally. Certain problem areas were identified such as cheating, the support systems for students who become stressed, teaching that over-emphasized factual learning, teaching being too teacher centered, and students' irritation with their teachers; these problems need to be examined more closely. In addition, other areas that require enhancement in the TUCOM educational environment were identified for effective management of learning especially in the students' perception of teachers and students perception of atmosphere sub domains.

**Key words:** Medical curricula, DREEM questionnaire, Educational environment, TUCOM, Iraq.

## Introduction

Environment of learning plays a critical role in how students learn and in the quality of learning outcomes [1, 2, 3]. Tikrit University College of Medicine is a government medical institution situated in Tikrit, Iraq. It was started in 1989, adopting innovative curriculum, a community-oriented, community-based program incorporating a problem-based learning approach [4]. Medical educators are agreed that an optimal climate is an important factor for effective learning to occur [5, 6]. Thus following any educational institution establishment, evaluation of the educational environment has been highlighted as the key to the delivery of high quality medical education [5,6]. The learning environment for medical students has been extensively investigated around the world, with a view to identifying strengths and weaknesses, to monitor change at times of curriculum reform, to compare learning environments across teaching sites and to compare staff and students' perceptions [7-11].

Global changes in medical education caused students' perceptions of their educational environment to receive special attention [12]. Health care services delivery is facing global changes which are mainly influenced by cost, thus subsequently lead to short duration of admissions, increased patient acuity and greater use of ambulatory services [11]. This may lead to a paradigm shift in health profession education toward primary health care and outpatient clinics.

Students' perceptions of the educational environment may represent a basis for implementing modifications to improve the learning climate. Students' perceptions of their educational environment have a significant impact on their behavior, academic progress, learning experiences and outcomes. Regular assessment and modification of the educational environment is a possible action that can be performed in medical education. However, it is essential to perform such evaluation by using a valid and reliable tool. Students' perception is one method for assessing the educational environment. Dundee Ready Educational Environment Measure (DREEM) is used to assess the educational climate [13-30].

This valuable tool was originally designed in English [16] and has been translated into various languages such as Arabic, Swedish, Greek and Spanish [22,23,27,28,31]. These researchers have shown that DREEM is internationally accepted as a useful tool to provide feedback on strengths and weaknesses of the educational climate at particular educational institutions. One of the important implications of DREEM is that it provides a standardized way for international comparisons between medical schools as well as allowing them to benchmark their educational climate [32]. In addition, it may locate areas of concern shared by the majority of students that might be unintentionally neglected by educators.

Reliability is broadly described as the consistency or reproducibility of a measurement over time and occasions and it can be gauged in the form of internal consistency

and stability [34]. The internal consistency of a tool is commonly measured and based on a single administration while the stability of a tool is measured based on multiple administrations on different occasions or time [34]. The DREEM has been reported to have a high level of internal consistency with the overall Cronbach alpha coefficient being more than 0.7 [16,22,23, 31, 34]. It was also found to have a high level of stability with a test-retest correlation coefficient of more than 0.8 [23]. Apart from this instance, none of the articles have so far reported its reliability among Iraqi medical students. To the best of our knowledge, no previous research has used the DREEM to assess students' perceptions regarding educational environment at medical colleges in Iraq. The aim of this study was to assess the perceptions of medical students concerning their educational environment at Tikrit University College of Medicine in Iraq.

## Objective

To measure students' perceptions of the educational environment of the TUCOM curriculum and to evaluate the internal consistency of the 50-item Dundee Ready Education Environment Measure (DREEM) Arabic version questionnaire.

## Materials and Methods

### Instrument:

The development and validation of the 50-item DREEM has been reported elsewhere [16]. Respondents score each item from 0 to 4 (4 = Strongly agree, 3 = Agree, 2 = Unsure, 1 = Disagree and 0 = Strongly disagree). Some items (4, 8, 9, 17, 25, 35, 39, 48 and 50) contain negative statements and are therefore reverse-coded when incorporated into scales. According to Roff et al. [16] individual items with a mean score of 3 or greater reflect a positive educational environment and are considered areas of strength for a school; values between 2 and 3 reflect areas that are neither strengths nor weaknesses but identify areas that could be enhanced; and items with a mean score below 2 are considered areas of weaknesses for a school of medicine. The DREEM yields a global score of up to 200 with its 50 items combined and has five subscales proposed by Roff et al. [16]: (1) Students' Perceptions of Learning (items 1, 7, 13, 16, 20, 22, 24, 25, 38, 44, 47 and 48), which addresses students' views of aspects of the teaching activities, such as whether they receive clear course objectives, and whether learning is student-focused and encourages active learning rather than being teacher-centred and stresses factual learning; (2) Students' Perceptions of Teachers (items 2, 6, 8, 9, 18, 29, 32, 37, 39, 40 and 50), which address students' views of the qualities of teachers, including their communication skills, whether they provide feedback to students and patients, their level of knowledge and their level of preparation for classes; (3) Students' Perceptions of their Academic Skills (items 5, 10, 21, 26, 27, 31, 41 and 45), which includes students' views of the learning strategies and problem-solving skills they have developed to prepare themselves for their profession; (4) Students' Perceptions of the Learning Atmosphere (items 11, 12, 17, 23, 30, 33, 34, 35, 36, 42, 43 and 49), which includes items addressing how relaxed the atmosphere is during lectures and ward teaching, whether teaching activities are motivating for students, and whether there are opportunities for students to develop

interpersonal skills; and (5) Students' Perceptions of the Social Environment (items 3, 4, 14, 15, 19, 28 and 46), which addresses students' views of the support systems available to those who become stressed, the school's accommodation for students, the quality of campus social life, and whether students are able to find friends at school.

**Sample:**

This cross-sectional study was conducted at TUCOM in November 2012. The questionnaire was administered to undergraduate medical students of training years 2 and 3. The DREEM was administered in paper form to students. The questionnaires were answered anonymously by students.

The study design was approved by the ethical committee of TUCOM that was now registered in USA [U.S. Department of Health and Human Services (HHS)& Registration of an Institutional Review Board (IRB)]. IORG #: IORG0006885, Institution: Tikrit University College of Medicine [TUCOM] OMB No. 0990-0279.

**Reliability:**

The method described by Cronbach [35] was used to measure scale reliability. Since alpha depends on both the length of the scale (the number of questions) and the correlation of the items within the scale (actual reliability), the Spearman-Browne formula,

$$\alpha \text{ subscale} = k\alpha \text{ scale} / [1+(k-1) \alpha \text{ scale}]$$

where k is the number of items of the subscale divided by the number of items of the overall scale [36,37], was used to estimate expected subscale alphas. Content validity was addressed by the original DREEM. Not willing to limit our ability to compare results internationally, we did not delete or add any items, change items, original order (randomly arranged), or rearrange subscales.[33]

**Statistical analysis**

The variables were described using means and standard deviations (SD). Comparisons of students of the various years were analyzed using t tests. Differences were considered statistically significant with a p value <0.05. The internal consistencies of the inventory and its subscales were calculated using the Statistical Package for Social Science (SPSS 11) and the results were expressed as alpha coefficients ranging from 0 to 1.

**Results**

Completed questionnaires were received from 88 out of 114 students (77.2 %) in year 3, 108 out of 150 students (72%) in year 2. One questionnaire in year 3 had missed answers for some items, thus it was excluded from analysis. So only 87 questionnaires for year 3 were analyzed. The overall response rate was 74%. Among respondents, 104 (53.3 %) were males and 91 (46.7%) were females.

Item	N	Mean	Std. Deviation
Q1. I am encouraged to participate during teaching sessions	195	2.4051	1.10527
Q7. The teaching is often stimulating	195	2.2513	1.13221
Q13. The teaching is student-centred	195	2.6872	1.13045
Q16. The teaching helps to develop my competence	195	2.6462	.94319
Q20. The teaching is well-focused	195	2.2718	.94322
Q22. The teaching helps to develop my confidence	195	2.4667	1.06619
Q24. The teaching time is put to good use	195	2.1436	1.07449
Q25. The teaching over-emphasizes factual learning	195	1.5538	1.03591
Q38. I'm clear about the learning objectives of the course	195	2.5744	.92967
Q44. The teaching encourages me to be an active learner	195	2.2923	1.07535
Q47. Long-term learning is emphasized over short-term learning	195	2.7487	1.10921
Q48. The teaching is too teacher-centred	195	1.8205	1.27368
<b>Sum of domain</b>		<b>27.86</b>	

Table 1: Perception of teaching / learning

Item	N	Mean	Std. Deviation
Q2. The teachers are knowledgeable	195	2.7179	.91236
Q6. The teachers adopt a patient-centred approach to consulting	195	2.4205	.87790
Q8. The teachers ridicule the students	195	2.5231	1.07609
Q9. The teachers are authoritarian	195	<b>1.7436</b>	.75019
Q18. The teachers have good communication skills with patients	195	2.3538	.90413
Q29. The teachers are good at providing feedback to students	195	2.3949	.93774
Q32. The teachers provide constructive criticism here	195	2.1487	.93248
Q37. The teachers give clear examples	195	2.5385	.95373
Q39. The teachers get angry in teaching	195	2.1487	1.09518
Q40. The teachers are well-prepared for their teaching sessions	195	2.4205	.91808
Q50. The students irritate the teachers	195	<b>1.5744</b>	1.29167
<b>Sum of domain</b>		<b>24.98</b>	

Table 2: Students' Perception of teachers

Item	N	Mean	Std. Deviation
Q5. Learning strategies that worked for me before continue to work for me now	195	2.2564	1.09163
Q10. I am confident about my passing this year	195	2.8718	.81795
Q21. I feel I am being well prepared for my profession	195	2.0872	1.07818
Q26. Last year's work has been a good preparation for this year's work	195	2.5231	1.04202
Q27. I am able to memorize all I need	195	2.4410	.91401
Q31. I have learnt a lot about empathy in my profession	195	2.6154	1.08920
Q41. My problem-solving skills are being well developed here	195	2.6513	.90897
Q45. Much of what I have to learn seems relevant to a career in healthcare	195	2.7846	1.05262
<b>Sum of domain</b>		<b>20.23</b>	

Table 3: Students' Academic perception

Item	N	Mean	Std. Deviation
Q11. The atmosphere is relaxed during ward teaching	195	2.1795	1.13682
Q12. This school is well time-tabled	195	2.0103	1.14419
Q17. Cheating is a problem in this school	195	<b>1.1795</b>	1.29773
Q23. The atmosphere is relaxed during lectures	195	<b>1.5846</b>	1.13826
Q30. There are opportunities for me to develop my interpersonal skills	195	2.5795	1.13863
Q33. I feel comfortable in class socially	195	<b>1.6205</b>	.98942
Q34. The atmosphere is relaxed during class/seminars/tutorials	195	2.3487	1.11292
Q35. I find the experience disappointing	195	2.2821	.94566
Q36. I am able to concentrate well	195	2.2718	.96483
Q42. The enjoyment outweighs the stress of the course	195	<b>1.7795</b>	1.24254
Q43. The atmosphere motivates me as a learner	195	2.0923	1.15397
Q49. I feel able to ask the questions I want	195	2.0462	1.25711
<b>Sum of domain</b>		<b>23.97</b>	

Table 4: Perception of atmosphere

Item	N	Mean	Std. Deviation
Q3. There is a good support system for students who get stressed	195	<b>1.4308</b>	1.05473
Q4. I am too tired to enjoy the course	195	<b>1.7949</b>	1.31171
Q14. I am rarely bored in this course	195	2.1487	1.14128
Q15. I have good friends in this course	195	3.4154	.85961
Q19. My social life is good	195	3.2256	.75325
Q28. I seldom feel lonely	195	2.5744	1.17023
Q46. My accommodation is pleasant	195	2.2718	1.41530
<b>Sum of domain</b>		<b>16.86</b>	

Table 5: Social perception

Domain [Maximum score]	Sum of items scores				P Value	Total	
	Year 3		Year 2			Mean [SD]	Percent
	Mean [SD]	Percent	Mean [SD]	Percent			
SPL [48]	27.49 [5.49]	57.27	28.16 [5.61]	58.67	NS	27.86 [5.55]	58.04
SPT [44]	24.17 [5.52]	54.93	25.64 [5.74]	58.27	NS	24.98 [5.68]	56.77
SASP [32]	19.56 [5.04]	61.13	20.77 [4.55]	64.91	NS	20.23 [4.80]	63.22
SPA [48]	24.19 [7.36]	50.39	23.80 [7.83]	49.58	NS	23.97 [7.60]	49.94
SSSP [28]	16.92 [3.96]	60.43	16.81 [3.87]	60.04	NS	16.86 [3.90]	60.21
DREEM inventory [200]	112.34 [22.24]	56.17	115.18 [22.67]	57.59	NS	113.91 [22.46]	56.96

SPL- Student perception of learning; SPT- Students perception of teachers; SASP- Students academic self perception; SPA- Students perception of learning atmosphere; SSSP- Students social self perception.

**Table 6: A comparison of subscales sum (domain) and full DREEM inventory among years 3 and 2 undergraduate TUCOM medical students**

Domain [Maximum scale]	Sum				P Value	Total	
	Year 3		Year 2			Mean [SD]	Percent
	Mean [SD]	Percent	Mean [SD]	Percent			
SPL [4]	2.291 [0.349]	57.27	2.346 [0.410]	58.67	NS	2.322 [0.359]	58.04
SPT [4]	2.197 [0.371]	54.93	2.331 [0.353]	58.27	NS	2.271 [0.346]	56.77
SASP [4]	2.445 [0.257]	61.13	2.596 [0.287]	64.91	NS	2.529 [0.263]	63.22
SPA [4]	2.016 [0.467]	50.39	1.983 [0.351]	49.58	NS	1.998 [0.392]	49.94
SSSP [4]	2.417 [0.762]	60.43	2.402 [0.695]	60.04	NS	2.409 [0.722]	60.21
MEAN TOTAL [4]	2.247 [0.458]	56.17	2.304 [0.451]	57.59	NS	2.278 [0.440]	56.96

SPL- Student perception of learning; SPT- Students perception of teachers; SASP- Students academic self perception; SPA- Students perception of learning atmosphere; SSSP- Students social self perception

**Table 7: A comparison of subscales mean values among years 3 and 2 undergraduate TUCOM medical students**

**Individual item scores**

The mean scores of individual items are shown in Tables 1-5. Scores for 10 out of 50 items (20%) were below 2, indicating areas of weaknesses of the TUCOM. Items 17, 3, 50, 23, and 33 had the lowest mean scores of the 50 items. The values for the majority of the items (96%) fell into the range that indicated aspects of the environment that would benefit from improvement (mean scores between 2 and 3). Two items (4%) had scores of 3 or greater and identified areas perceived as contributing to a good educational environment by students: items 15, 19, 10, 45 and 7 were the five that received the highest mean scores.

Mean response values for 30 (60%) of the individual items were lower for students of year 3 than for students of year 2 (data not shown).

Regarding the students' perceptions of learning, there was a significant difference between year 3 and year 2 in items 7 (P=0.008), 20 (P=0.037), 25 (P=0.000) and 38 (P=0.029). In addition, there was a significant difference between males and females for items 13 (P=0.036). Furthermore, significant differences were observed for items 13 (P=0.025), 38 (P=0.008) and 47 (P=0.046) between students who entered the college through a central channel and those who come from colleges outside the country.

Domain [Maximum score]	Sum				P Value	Total	
	Male		Female			Mean [SD]	Percent
	Mean [SD]	Percent	Mean [SD]	Percent			
SPL [48]	28.41 [5.46]	59.19	27.23 [5.62]	56.73	NS	27.86 [5.55]	58.04
SPT [44]	24.67 [6.03]	56.10	25.34 [5.26]	57.59	NS	24.98 [5.68]	56.77
SASP [32]	20.86 [4.53]	65.19	19.51 [5.01]	60.97	NS	20.23 [4.80]	63.22
SPA [48]	25.50 [7.72]	53.13	22.23 [7.11]	<b>46.31</b>	NS	23.97 [7.60]	49.94
SSSP [28]	16.71 [3.73]	59.68	17.03 [4.10]	60.82	NS	16.86 [3.90]	60.21
DREEM inventory [200]	116.16 [22.75]	58.08	111.34 [21.98]	55.67	NS	113.91 [22.46]	56.96

SPL- Student perception of learning; SPT- Students perception of teachers; SASP- Students academic self perception; SPA- Students perception of learning atmosphere; SSSP- Students social self perception.

**Table 8: A comparison of subscales sum (domain) and full DREEM inventory among years 3 and 2 undergraduate TUCOM medical students according to gender**

Domain	3 <sup>rd</sup> year		2 <sup>nd</sup> year	
	Mean [ ± SD]		Mean [ ± SD]	
	Male	Female	Male	Female
SPL	2.269 [0.348]	2.325 [0.379]	2.473 [0.563]	2.238 [0.341]
SPT	2.148 [0.296]	2.303 [0.521]	2.364 [0.341]	2.303 [0.376]
SASP	2.467 [0.260]	2.407 [0.292]	2.760 [0.316]	2.456 [0.267]
SPA	2.014 [0.452]	2.015 [0.503]	<b>2.243</b> <b>[0.381]</b>	<b>1.755</b> <b>[0.361]</b>
SSSP	2.338 [0.846]	2.550 [0.676]	2.442 [0.723]	2.367 [0.750]
Total	2.182 [0.408]	2.290 [0.422]	2.435 [0.488]	2.189 [0.420]

 P=0.003

SPL- Student perception of learning; SPT- Students perception of teachers; SASP- Students academic self perception; SPA- Students perception of learning atmosphere; SSSP- Students social self perception

**Table 9: Educational Environment comparison between males and females for 3rd and 2nd years TUCOM students**

In terms of students' perceptions of teachers, items 2, 8 and 50 show significant ( $P=0.001$ ,  $0.027$  and  $0.019$  respectively) differences between 3rd and 2nd year. In addition, significant gender differences were achieved for items 2 ( $P=0.046$ ), 9 ( $P=0.025$ ) and 40 ( $P=0.046$ ). Regarding the students' academic perceptions, item 10 was significantly different between male and female ( $P=0.012$ ) and between 3rd and 2nd year ( $P=0.000$ ).

Concerning students' perceptions of atmosphere, there were significant differences demonstrated by gender for items 23 ( $P=0.04$ ), 30 ( $P=0.003$ ), 33 ( $P=0.004$ ), 34 ( $P=0.007$ ) and 36 ( $P=0.000$ ). A significant difference between year 3 and 2 was observed for item 17 ( $P=0.006$ ) only. For acceptance channel, only item 30 demonstrated a significant ( $P=0.014$ ) difference.

Regarding students' social perceptions, gender demonstrated significant differences for items 15 ( $P=0.02$ ) and 46 ( $P=0.000$ ). In addition, the acceptance channel shows significant differences for items 15 ( $P=0.031$ ), 19 ( $P=0.029$ ), 28 ( $P=0.035$ ) and 46 ( $P=0.006$ ).

#### Subscales and overall mean scores:

The 5 subscales and overall mean scores according to study years are shown in Table 6. The subscale with the highest mean score was students' perceptions of their academic skills:  $20.23 \pm 4.8$  out of 32, corresponding to 63.22% of the maximum score. The lowest mean score was for the students' perceptions of the college atmosphere:  $23.97 \pm 7.6$  (49.94% of the maximum score). Scores observed for year 3 students were lower in subscales SPL, SPT, and SASP compared to year 2, but the difference was not statistically significant. The overall mean score for the 50 items was  $113.91 \pm 22.46$  (56.96%). Students of year 2 had the higher mean score with  $115.18 \pm 22.67$ , while year 3 overall mean value was  $112.34 \pm 22.24$ , with no significant difference.

The subscales and mean scores according to study years are shown in Table 7. The subscale with the highest mean score was SASP:  $2.529 \pm 0.263$  out of 4, corresponding to 63.22% of the maximum score. The lowest mean score was for the SPA:  $1.998 \pm 0.392$  (49.94% of the maximum score). Scores observed for year 3 students were lower in subscales SPL, SPT, and SASP compared to years 2, but the difference was not statistically significant. The overall mean score for the 50 items was  $2.278 \pm 0.44$  (56.96%). Students of year 2 had the higher mean score with  $2.304 \pm 0.451$ , while year 3 overall mean value was  $2.247 \pm 0.458$ , with no significant difference.

The gender based difference was observed with regard to teaching being sufficiently concerned to develop competence in the students' perception of learning subscale (Male,  $28.41 \pm 5.46$ , 59.19% vs. female,  $27.23 \pm 5.62$ , 56.73%). Table 8. However the difference was not significant. The same findings were observed for SASP and SPA. In contrast, females have a higher mean score of SPT & SSSP subscales (Table 8). The overall mean score for DREEM 50 items was higher in males ( $116.16 \pm 22.75$ ) compared to female s ( $111.34 \pm 21.98$ ), but the difference was not significant.

When the data was subdivided according to gender and study years, gender based significant difference was observed with regard to atmosphere ( $P=0.003$ ), with a negative value toward female (Male,  $2.243 \pm 0.381$ ; female  $1.1755 \pm 0.361$ ) Table 9.

#### Reliability

Internal consistency findings are shown in Table 10. The 50-item DREEM Arabic version was found highly reliable, with an alpha coefficient of 0.91 in year 3, 0.91 in year 2 ( $p=NS$  for difference in alphas across years). The internal consistency of the inventory among all 195 respondents was 0.91. Internal consistencies of the five subscales were found to reflect adequate reliability, although the coefficient for Perceptions of the Social Environment was lower than that of the other subscales indicating its poorer reliability. Internal consistency for gender was 0.91 for both sexes.

#### Comparison to standards:

Table 11 shows the comparison of these study findings with standards as suggested by McAleer & Roff [38]. The overall DREEM score indicates that the education environment in TUCOM was more positive than negative. The students' perceptions of learning score indicated that teaching was viewed positively, since the score was more than 24, which represents the upper limit score value of negative teaching view. Students' perceptions of teachers were moved in the right direction. SASP score indicated that students feeling on the positive side. In addition, SSSP score suggests that TUCOM society is not too bad. In contrast, the study indicated a more negative atmosphere.

#### Discussion

The overall alpha was much higher than the 0.7 [37] or 0.80 [33] threshold generally considered acceptable for scales. The DREEM questionnaire used in this study was found to be an internally reliable instrument for measuring students' views of the educational climate of a TUCOM. The 50-item DREEM Arabic version was found to have a similar reliability coefficient (Cronbach alpha) to published studies of the DREEM translation in different languages [22,23,27,28,31, 39, 40,41]. Furthermore, DREEM had a high alpha coefficient when analyzed in regards to gender and year of study, a similar finding to that reported for Greece [23]. However, the alpha coefficients of each subscale were lower than the overall reliability, ranging from 0.49 to 0.75. The lowest reliability was obtained by the Students' Social Self-Perceptions in agreement with other studies [22, 23,40] who obtained very similar alpha coefficients for the subscales and full inventory in India, Spain and Greece. Psychometric analyses of the instrument were carried out by de Oliveira Filho et al. [41] in postgraduate training programmes in Brazil. They found the DREEM inventory valid, with high discriminant and concurrent validities and high reliability with an alpha coefficient of 0.93 and generalizability coefficient of 0.95.

The individual items' mean scores offered an opportunity to improve certain areas of the TUCOM educational environment that were perceived by students as weaknesses, including the support systems for students who become stressed, cheating as a problem in the college, teaching

Domain	Standard McAleer & Roff [score] (2002)	Our score	Interpretation
DREEM overall	More positive than negative [101-150]	113.91	P > N
SPL	Teaching viewed negatively [13-24]	27.86	TVP
SPT	Moving in the right direction [23-33]	24.98	MRD
SASP	Feeling more on the positive side [17-24]	20.23	FPS
SPA	More positive atmosphere [25-36]	23.97	More Negative Atmosphere
SSSP	Not too bad [15-21]	16.86	NTB

Table 10: Comparison of the subscales with the standards values

Scale	Items	Number	Alpha
<b>Overall DREEM</b>	<b>50</b>	<b>195</b>	<b>0.91</b>
Subscale	Learning	12	0.60
	Teachers	11	0.75
	Academic	8	0.74
	Atmosphere	12	0.81
	Social	7	0.49
Gender	Male	50	0.91
	Female	50	0.91
Year of study	3	50	0.91
	2	50	0.91

Table 11: Cronbach’s alpha for different scales and subscales

that over-emphasized factual learning, teaching being too teacher centered, and students’ irritation with their teachers. Analysis of individual items also proved to be a useful tool for recognizing areas where the educational environment was good, such as the quality of the college teachers in terms of their medical knowledge and teaching abilities. Furthermore, individual analysis addressed the areas that require enhancement; 19 items with mean score of lower than 2.4 (60% of score value require reform for their enhancement. However, another 10 items represent a problem in the educational process in TUCOM. Thus these 29 items should be considered by the college administration for reform, change and enhancement.

The female students scored more negatively on several aspects of educational environment than males (35/50 items). However, males perceived more loneliness. Gender differences reported in other studies with female students perceiving the learning environments as less supportive than their male counterparts [7,30,42] agreed with our findings. The present study findings contrast with others [11,20,29].

The analysis of the subscales showed a high mean score for students’ academic perceptions. The teacher’s confidence in

their ability to teach is not supported by the views of their students. The mean score of the subscale, students perceptions of their teachers, was the 4th of all (5) subscales. This finding is consistent with the item analysis and may reflect that the staff development programs were not designed properly. The college administration is not interested in staff training and development. The other subscales that reflected a positive educational environment were students’ perceptions of their academic skills and their perceptions of their learning. On the other hand, students’ perceptions of teachers and of the learning atmosphere revealed domains of the educational environment that could stand improvement.

Three of the five subscales mean scores of students in year 3 were lower than the mean scores for students in year 2. This may be due to differences in the physical environments, proportion of clinical activities and proportion of mature students or validity of the instrument used to measure the educational environment [43, 44]. Al-Hazimi et al. [14] analyzed the educational environment at three schools of medicine: two with traditional curricula in Saudi Arabia and the Republic of Yemen, and a third, Scottish medical school with an innovative curriculum as defined by the GMC in the UK [45]. The Scottish medical school obtained an overall

DREEM score of 139, significantly higher than the scores obtained by the traditional universities, which were 100 and 107. However, an innovative curriculum design is not the only factor related to a good educational environment. Curriculum changes are usually undertaken in order to improve the overall learning environment for students; the process, however, is often stressful for both students and faculty [16, 46].

The TUCOM obtained an overall mean score of 113.91, which is considered an indication of a generally positive educational environment. The DREEM scores obtained by students in year 3 and 2 were comparable with DREEM scores reported by UK medical schools with curricula aligned with the recommendations suggested by the GMC in Tomorrow's Doctors [14,16,19]. Roff [30] pointed out that "It remains to be established if the type of curriculum offered by a given school can be 'detected' by the DREEM". However, a higher DREEM score indicates a more student-centred curriculum, and schools with traditional curricula commonly score less than 120 [14,19].

DREEM has proven to be a useful tool for identifying the strengths and weaknesses of the TUCOM's curriculum. The results presented herein revealed a mean overall score of 113.91/200 for the DREEM items. According to the practical guide of McAleer and Roff [38], a mean score between 50 and 100 indicates potential problems. The overall DREEM score indicated that the education environment in TUCOM was more positive than negative. For the students' perceptions of learning score indicating that teaching was viewed positively, the score was more than 24, which represents the upper limit score value of negative teaching view. Students' perceptions of teachers were moved in the right direction. SASP score indicated students feeling on the positive side. In addition, SSSP score suggests that TUCOM society is not too bad. In contrast, the study indicated a more negative atmosphere.

In 2003-2010 the field work curriculum was reduced due to many factors and subsequently this gap is filled with theoretical teaching. This means that curriculum implementation was deviated from its design. In the mean time college administration tried to reform the curriculum and return back to its sound implementation. In the meantime the college curriculum implementation needs to be devoted to field training and ambulatory clinical practice. The assessment system needs improvement by expansion of its use of Objective Structured Clinical Examinations (OSCE) and to introduce portfolios in order to minimize assessments of students' factual recall of information. The present study findings should be analyzed in depth by the focus group of students and teachers of the TUCOM in the context of the college's accreditation process. The purpose of such analyses by the Focus groups were to clarify the underlying causes for areas with poor scores, which varied by student-year, and gender group. Stress resulting from experiences on clinical placements was highlighted by some students and cheating in written examinations was confirmed as a general problem, although not for OSCE.

In Table 12, we compare the results of this study with other published data. Such comparison may not be valid as these studies were carried out in different years, and different environments. [20,22,23,24-30]. Nevertheless, our results indicated that global mean score (113.91) was lower than that reported for UK [16,30] Nepal [25], Spain [22] and Nigeria [25]. However, our global score was higher for Canada [7], Trinidad [26], Saudi Arabia [27,28] Iran [20], Greece [23] and Sri Lanka [29]. Our results rank 4th for SSSP, 5th for SASP, 7th for SPL, 8th for SPT, and 10th for SPA.

However, DREEM has proven to be a useful tool for identifying the strengths and weaknesses of the TUCOM's curriculum. The qualitative data collected by a focus group have substantially enhanced questionnaire interpretation, allowing us to undertake remedies to address common causes for student dissatisfaction. This approach of combining DREEM results and qualitative analysis using focus groups and open ended questions has been recommended by Whittle et al. [47] as an approach to improving the educational environment and the overall quality of students' education. In the future, the DREEM questionnaire could again be administered in TUCOM to measure the impact of current and future changes in the curriculum on students' perceptions of their educational environment.

Based on this study's findings, we recommend the 50-item DREEM Arabic version as a reliable instrument for other Iraqi Medical Colleges' students. It can be used to identify an institution's strengths and weaknesses, make comparisons of students' perceptions of educational environments within an institution (like identifying changes in perceptions over time) and between students of different medical schools. It can also be used to assess the correlation of the overall mean score of the DREEM questionnaire with students' academic performance reflected in their grade point averages, and serve as a tool to identify students who are likely to be academic achievers and those who are at risk of poor academic performance [30].

## Conclusion

The DREEM is a reliable and practical tool for assessing the educational environment in Iraqi Medical Colleges. The learning environment of TUCOM is perceived positively and our students perspectives compare favorably with studies internationally. Certain problem areas were identified such as cheating, the support systems for students who become stressed, teaching that over-emphasized factual learning, teaching being too teacher centered, and students irritation with their teachers; these problems need to be examined more closely. In addition, other areas that require enhancement in the TUCOM educational environment were identified for effective management of learning especially in the students' perception of teachers and students' perception of atmosphere sub domains.

Year, Country, [reference]	Overall	SPL	SPT	SASP	SPA	SSSP
1997, UK, [16]	66.2	65.8	65.8	64.3	68.6	65.4
2001, Nigeria [25]	59.0	68.8	59.1	65.6	56.3	46.4
2001, Nepal [25]	65.0	68.8	59.1	68.8	66.7	64.3
2002, Trinidad [26]	55.0	58.3	53.6	58.8	52.2	51.6
2004, Canada [7]	48.5	39.6	54.5	46.9	52.1	53.6
2004, Saudi Arabia [27]	51.1	45.8	45.5	53.1	47.9	53.5
2005, Saudi Arabia [ 28]	45.0	40.7	48.3	46.3	44.4	46.3
2009, Sudan [24]	49.75	53.12	59.24	54.9	38.8	42.2
2010, Iran [20]	49.8	44.2	55.0	49.4	49.6	51.8
2012, Spain [22]	63.8	59.8	68.9	69.7	62.9	56.8
2012, Greece [23]	53.8	47.5	57.7	52.2	56.9	55.7
2010, Sri Lanka [29]	53.7	56.0	51.7	56.9	51.5	53.1
Scotland [30]	69.5	70.8	65.9	71.9	72.9	71.4
<b>2013, TUCOM This study</b>	<b>56.96</b>	<b>58.04</b>	<b>56.77</b>	<b>63.22</b>	<b>49.9</b>	<b>60.2</b>

Table 12: Comparison with other studies [Percent]

## References

- Konings K, Brand-Gruwel S, Merrienboer J. Towards more powerful learning environments through combining the perspectives of designers, teachers and students. *Br J Psychol Medicine* 2005;75:645-660.
- Hutchison L. Educational Environment. *BMJ* 2003;326:810-812.
- Hoffman KG, Donaldson JF. Contextual tensions of the clinical environment and their influence on teaching and learning. *Med Educ* 2004;38:448-454.
- Alsamarai AG, Alsheikh GY. Medical education in Iraq: Curriculum of Tikrit University College of Medicine as an example. Part. I. *Ann Iraqi Sci* 2008;1(1)129-135.
- Dent, J. A., & Harden, R. M. A practical guide for medical teachers (3rd ed.): Elsevier Churchill Livingstone. 2009.
- Newble, D., Cannon, R. A., & Kapelis, Z. A. A handbook for medical teachers: Kluwer Academic Publishers. 2001.
- Till H. Identifying the weaknesses of a new curriculum by means of the Dundee Ready Education Environment Measure (DREEM) Inventory. *Med Teach* 2004;26910:39-45.
- Edgren G, Haffling A, Jakobsson U, et al. Comparing the educational environment (as measured by the DREEM) at two different stages of curriculum reform. *Med Teach* 2010;32: e233-238.
- McKendree J. Can we create an equivalent educational experience at a two campus medical school? *Med Teach* 2009; 31:e202-205.
- Miles S, Leinster S. Comparing staff and student perceptions of the student experience at a new medical school. *Med Teach* 2009;31:539-546.
- Pinnock R, Shulruf B, Hawken SJ, Hening MA, Jones Rhys. Students' and teachers' perceptions of the clinical learning environment in year 4 and 5 at the University of Auckland. *NZ Med J.* 2011;124:63-70.
- Miles S, Leinster SL: Medical Students' perceptions of their educational environment: expected versus actual perceptions. *Med Educ* 2007, 41(3):265-72.
- Al-hazimi, A., Al-hyiani, A., & Roff, S. Perceptions of the educational environment of the medical school in King Abdul Aziz University, Saudi Arabia. *Medical Teacher*,2004; 26(6), 570-573.
- Al-Hazimi, A., Zaini, R., Al-Hyiani, A., Hassan, N., Gunaid, A., Ponnampuruma, G., et al. Educational environment in traditional and innovative medical schools: A study in four undergraduate medical schools. *Edu for Health* 2004. 17(2), 192-203.
- Arzuman, H., Yusoff, M. S. B., & Chit, S. P. Big Sib Students' Perceptions of the Educational Environment at the School of Medical Sciences, Universiti Sains Malaysia, using Dundee Ready Educational Environment Measure (DREEM) Inventory. *Malaysian Journal of Medical Sciences*,2010; 17(3), 40-47.
- Roff, S., McAleer, S., Harden, R. M., Al-Qahtani, M., Ahmed, A. U., Deza, H., et al. Development and validation of the Dundee ready education environment measure (DREEM). *Medical Teacher*, 1979;19(4), 295-299.
- Said, N. M., Rogayah, J., & Arzuman, H. A study of learning environments in the Kulliyah (Faculty) of Nursing, International Islamic University Malaysia. *Malaysian Journal of Medical Sciences*, 2009;16(4), 15-24.
- Thomas, B. S., Abraham, R. R., Alexander, M., & Ramnarayan, K. Students' perceptions regarding educational environment in an Indian dental school. *Medical Teacher*, 2009;31(5), 185-188.
- Varma, R., Tiyagi, E., & Gupta, J. Determining the quality of educational climate across multiple undergraduate teaching

- sites using the DREEM inventory. *BMC Medical Education*, 2005;5(1), 8.
20. Aghamolaei T, Fazel I. Medical students perceptions of the educational environment at the Iranian medical sciences university. *BMC Med Edu* 2010;10:87-94.
21. Brown T, Williams B, Lynch M. The Australian DREEM: Evaluating student perceptions of the academic learning environments within eight health science courses. *Int J Med Edu* 2011;2:94-101.
22. Riquelme, A., Oporto, M., Oporto, J., Mendez, J. I., Viviani, P., Salech, F., et al. Measuring students' perceptions of the educational climate of the new curriculum at the Pontificia Universidad Catolica de Chile: performance of the Spanish translation of the Dundee Ready Education Environment Measure (DREEM). *Education for health* (Abingdon, England), 2009;22(1), 112
23. Dimoliatis, I., Vasilaki, E., Anastassopoulos, P., Ioannidis, J., & Roff, S. Validation of the Greek translation of the Dundee ready education environment measure (DREEM). *Education for Health*, 2010;23(1), 348.
24. Baldo MH, Alobaid SE, Dadr IA. Measuring the medical educational environment at Alzaiem Alazhari University. *Khartoum Med J* 2010;3:500-507.
25. Roff S, McAleer S, Ifere OS, Bhattacharya S. A global diagnostic tool for measuring educational environment comparing Nigeria and Nepal, *Medical teacher*, 2001; 23: 378-82.
26. Bassaw B, Roff S, McAleer S, Roopnarinesing S, Delisle J, Teelucksingh S, Gopaul S. Students' perspectives on the educational environment. *Faculty of Medical Sciences. Trinidad Medical Teacher*, 2003; 25:522-6
27. Al Hazmi A, Al Hayiani A, Roff S. Perceptions of the educational environment of the medical school of King Abdul Aziz University, Saudi Arabia, *Medical Teacher* 2004; 26:570-3.
28. Al-Ayed, I.H. Sheikh SA. Assessment of the educational environment at the College of Medicine of King Saud university, Riyadh. *The Eastern Mediterranean Health Journal*, WHO. 2008;4:953-959.
29. Lokuhetty MD, Warnakulasuriya SP, Perera RI, Silva H, Wijesinghe HD. Students perceptions of the educational environment in a medical faculty with an innovative curriculum in Sri Lanka. *South-East Asian J Med Edu* 2010;4:9-16.
30. Roff, S. The Dundee Ready Education Environment Measure (DREEM) - a generic instrument for measuring students' perceptions of undergraduate health profession curricula, *Medical Teacher*, 2005;27(4), pp. 322-325.
31. Jakobsson, U., Danielsen, N., & Edgren, G. Psychometric evaluation of the Dundee Ready Educational Environment Measure: Swedish version. *Medical Teacher*, 2011;33(5), 267-274.
32. Hammond, S. M., O'Rourke, M., Kelly, M., Bennett, D., & O'Flynn, S. A psychometric appraisal of the DREEM. *BMC Medical Education*, 2012;12(1), 2.
33. Streiner, L. D., & Norman, G. R. *Health Measurement Scales: A Practical Guide to Their Development and Use* (4th ed.). New York: Oxford University Press. 2008.
34. Khan, J. S., Tabasum, S., Yousafzai, U. K., & Fatima, M. DREEM ON: Validation of the Dundee Ready Education Environment Measure in Pakistan. *J Pak Med Assoc*, 2011;61(9), 885-888
35. Cronbach L.J. Coefficient alpha and the internal structure of tests. *Psychometrika*, 1951;16, 297-334.
36. Norusis/SPSS Inc. *SPSS Professional Statistics™ 7.5. Chapter 13 Measuring scales: reliability analysis examples*; 1997. p. 103-111.
37. Fayers PM, Machin D. *Quality of life: assessment, analysis and interpretation*. John Willey & Sons. England; 2000.
38. McAleer S, Roff S. Part 3; A practical guide to using the Dundee Ready Education Measure (DREEM). In, J. M. Genn (ed), *AMEE Medical Education Guide No.23 Curriculum, environment, climate, quality and change in medical education; a unifying perspective*. Dundee, UK: Association of Medical Education in Europe; 2002.
39. Pimpayon P, Roff S, McAleer S, Poonchai B, Pemba S. Educational environment, student approaches to learning and academic achievement in a Thai nursing school. *Medical Teacher*. 2000; 22:359-365.
40. Mayya S, Roff S. Students' Perceptions of Educational Environment: A Comparison of Academic Achievers and Under-Achievers at Kasturba Medical College, India. *Education for Health*. 2004; 17(3), 280-291.
41. de Oliveira Filho GR, Vieira JE, Schonhorst L. Psychometric properties of the Dundee Ready Educational Environment Measure (DREEM) applied to medical residents. *Medical Teacher*. 2005; 27(4):343-347.
42. Jiffry M T, McAleer S, Fernando S, Marasinghe RB. Using the DREEM questionnaire to gather baseline data information in an evolving medical school in Sri Lanka, *Med Teach* 2005;27(4):348-352
43. Wangsaturaka D. Development of Learning Climate Measures for Thai Medical Education. PhD thesis, Faculty of Medicine, Dentistry and Nursing, University of Dundee. 2005.
44. Roff S., McAleer, S. & Skinner A. Development and validation of an instrument to measure postgraduate clinical learning and teaching educational environment for hospital-based junior doctors in the UK. *Medical Teacher*, 2005;27(4), 326-331.
45. GENERAL MEDICAL COUNCIL. *Tomorrow's Doctors. Recommendations on Undergraduate Medical Education*, London, General Medical Council. 1993.
46. McAleer S., Roff S., Harden R.M., Al-Qahtani M., Uddin A.A., Deza H. & Groenen G. The medical education environment measure; a diagnostic tool. *Medical Education*, 1998; 32(2), 217.
47. Whittle, S., Whelan, B. & Murdoch-Eaton, D.G. DREEM and beyond; studies of the educational environment as a means for its enhancement, *Education for Health*, 2007;20(1): 7.

# Transient Neonatal pustular melanosis: A Retrospective Review

## ABSTRACT

**Background:** Transient Neonatal pustular melanosis is the common, transient, benign, self limiting, asymptomatic skin rash in healthy newborns in the early neonatal period. It is characterized by pustules and evolves into areas of macular pigmentation.

**Objective:** The aim of this study is to describe the epidemiology, clinical manifestation, differential diagnosis, therapy, and outcome of Transient Neonatal pustular melanosis at KHMC and Queen Rania Childrens hospital and Prince Rashed hospital.

**Methods:** The present study was based on newly diagnosed cases presenting to the outpatient clinic of pediatric dermatology clinics at KHMC, Queen Rania Hospital for Children and Prince Rashed hospital between February 2008 and March 2013.

All subjects up to the age of one week were included. Extracted data include duration of pregnancy, type of delivery, age, sex, cutaneous rash characteristics, associated clinical conditions, laboratory investigations, skin biopsy, and treatment.

Simple statistical analyses (mean, frequency, and percentage) were used to describe the study variables.

**Results:** The study included 114 patients, 60 males and 54 females with a male to female ratio of 1.1:1. The age at onset of the rash ranged from 1 to 7 days (mean age was 3 days). All subjects were products of hospital-based deliveries. The flaccid, superficial fragile pustules, with no surrounding erythema were the commonest 83 (72.8%) cases, 27 (23.7%) cases presented with slightly hyperpigmented macules with fine collarette scale of site of ruptured and resolving pustules, 4 (3.5%) cases with pigmented maculae already present at birth. Affected infants are otherwise entirely well. Total blood count and Tzanck smear were done in 38 (33.3%) subjects. Skin biopsy was done in 2 (1.8%) cases. History of drug intake during pregnancy was found in about two thirds of cases (66.7%). All patients required no treatment and the rash disappeared. Follow up was done at 4 weeks of age.

**Conclusion:** Transient Pustular melanosis is usually a self-limiting disease and without long term sequelae so there is need to spare a healthy neonate with a benign transient condition from invasive evaluations for sepsis, harmful antibiotic therapy and prolonged hospitalization.

**Key Words:** Transient pustular melanosis, lentiginos Neonatorum, sterile, transient neonatal pustulosis.

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### Introduction

Transient Neonatal pustular melanosis, a benign idiopathic skin condition, mainly seen in newborns, is characterized by pustules that are present at birth and evolve into areas of macular pigmentation.(1-5,8-11,13-16,18,19,21)

It occurs in 4-5% of African/ American and 0.5% Caucasian newborns who are full term.(1, 2, 8, 9, 16, 19)

It clinically manifests in three phases, with superficial vesiculopustules that occur on the chin, neck, forehead, chest, buttocks, back, and less often on the palms and soles. The second phase is resolution of pustules with surrounding fine white collarettes of scale. The final phase is residual hyperpigmented macules.(1, 2, 9, 10, 11, 13-16,19, 22)

At 48 hours after birth few pustules remained, the established lesions showed peripheral desquamation, and the newborn presented excellent general health.(4)

At 4 days the condition has resolved, with only hyperpigmented macules visible in areas where the pustules had been.(4)

Transient Neonatal pustular melanosis is a rare disorder with worldwide prevalence in newborn infants of less than 1%.(4)

It affects both sexes equally and is more common in black infants (4.4%). (3, 8, 10, 16)

The aetiology of Transient Neonatal pustular melanosis is unknown and no association with maternal infections or exposure to toxic substances has been detected.(2, 3, 8, 11, 14, 19)

The initial lesions usually disappear spontaneously within the first two weeks of life, and no treatment is required.(1-4, 14)

The pustules rupture and leave hyperpigmented macules with collarette scaling that persists several weeks and even months. (1, 3, 4, 8-10, 14, 16, 19, 22)

The diagnosis based on clinical findings and typical lesions are usually easily diagnosed; therefore laboratory investigations are often not necessary. However when investigations are performed it is often to screen for other serious conditions that require urgent antibiotic treatment.(1-5, 8, 9, 14, 16)

Tzank cytological smear of the pustule content demonstrates inflammatory cells, predominantly neutrophils and bacterial culture negative.(4, 8, 9, 14, 16, 19, 22)

The pathology of Transient Neonatal pustular melanosis is usually performed in a limited number of cases which present as subcorneal or intraepidermal pustules composed mainly of neutrophils and a few eosinophils. The pigmented macules demonstrate basal and suprabasal increase in pigmentation only.(1, 2, 5, 6-7, 9, 12, 14, 16, 17)

Originally described in 1961 as lentignes Neonatorum, the full diagnosis of Transient Neonatal pustular melanosis was not recognized until 15 years later. (1)

Transient Neonatal pustular melanosis was first described by Ramamurthy et al. in 1976.(8,15)

Perrin et al. discovered a higher incidence of squamous metaplasia of the placenta in the mothers of affected children than in mothers in control infants. This finding has not subsequently been confirmed, and there are currently no arguments to link TPM to an infectious process. The higher incidence in black neonates may be related to an accelerated stimulation of negroid melanocytes due to cytokines and to release of growth factor by cells in the epidermal infiltrate.(2, 3)

The aim of this review was to describe epidemiology, clinical manifestations, differential diagnosis, and treatment outcome of transient neonatal pustular melanosis in healthy newborns at King Hussein Medical Centre, Queen Rania Children Hospital and Prince Rashed hospital.

## Methods

The present study was based on newly diagnosed cases presenting to the outpatient clinic of pediatric dermatology clinics at KHMC and Queen Rania Hospital for Children and Prince Rashed hospital between February 2008 and March 2013.

All subjects up to the age of one week were included. Extracted data included duration of pregnancy, type of delivery, age, sex, cutaneous rash characteristics, associated clinical conditions, differential diagnosis, laboratory investigations, skin biopsy, and treatment.

Simple statistical analyses (mean, frequency, and percentage) were used to describe the study variables.

## Results

The study included 114 patients, 60 males and 54 females with a male to female ratio of 1.1:1. The age at onset of the rash ranged from 1 to 7 days (mean age was 3 days). All subjects were products of hospital-based deliveries and breastfed.

Table 1 shows the study parameters and clinical manifestations with the flaccid, superficial fragile pustules, with no surrounding erythema, were the commonest 83 (72.8%) cases; 27 (23.7%) cases presented with the second phase resolution of pustules with surrounding fine white collarettes of scale and 4 (3.5%) cases with pigmented maculae already presented at birth. Mothers of 78 (66.7%) patients admitted to (unspecified) drug intake during pregnancy.

Affected infants were otherwise entirely well. Normal blood count was evident in complete blood count in 38 (33.3%) patients with severe pustular skin rash.

High polymorphonuclear leukocytes count was evident in Tzanck cytological smear from the pustules of 38 (33.3%) patients with severe pustular skin rash.

Histological examination showed typical sub corneal accumulations of polymorphonuclear leucocytes and scattered eosinophils in skin biopsy of 2 (1.8%) patients with severe pustular skin rash, poor feeding and low grade fever.

All patients required no treatment and the rash disappeared within 4 days. Follow up was done for 4 weeks of age with no permanent sequelae in any of the involved subjects.

## Discussion

Transient Neonatal pustular melanosis is a rare disorder with worldwide prevalence in newborn infants of less than 1%.(4)

The articles about Transient Neonatal pustular melanosis are few, because of the rarity of the disease and its short period of clinical manifestation.

Most of our cases had the onset of Transient Neonatal pustular melanosis at 48 hours after delivery, in full term infants; this is in agreement with most studies.(1-5, 8-10, 13-16, 18-19, 21)

In our study the prevalence of Transient Neonatal pustular melanosis is 0.4%, this is in agreement with most studies. (1-3, 8-11, 14, 16, 19, 21, 22.)

This study showed the predominance of male patients with a ratio of 1.1:1. This is not in agreement with other studies. (3, 8, 10, 16)

The most common skin rash type was pustular in 83 (72.8%) followed by 27 (23.7%) cases who presented with resolution of pustules with surrounding fine white collarettes of scale. This is similar to other studies. (1-2,9-11,13-16,19,22 )

Entity	Number	Percentage %
Sex		
Males	60	52.6%
Females	54	47.4%
Flaccid , superficial fragile pustules	83	72.8
Resolution of pustules with surrounding fine white collarettes of scale.	27	27.3
Pigmented maculae already presented at birth	4	3.5
Skin rash with low grade fever and poor feeding	2	1.8
History of drug intake during pregnancy	78	66.7
Complete blood count	38	33.3
Tzanck smear	38	33.3
Skin biopsy	2	1.8
Skin culture from pustular pustules	2	negative

Table 1: Demographic data and clinical manifestation among the study group



Figure 1: Pustular skin rash.

Severe pustular skin rash was noted in two subjects (1.8%), who also had low grade fever and poor feeding. The main differential diagnosis in these cases is bacterial infection.(4, 17) CBC from these patients showed normal peripheral blood count and pus cultures yielded negative results. Tzanck cytological smears and skin biopsy were performed in these patients, where the diagnosis of Transient Neonatal pustular melanosis was confirmed and the skin rash and fever disappeared without treatment as well as in

other patients with Transient Neonatal pustular melanosis. The presence of severe skin rash and fever in patients with Transient Neonatal pustular melanosis has not been mentioned and is not expected due to the non-infectious nature of the condition. Its presence in our subjects triggered the investigations that were performed in the affected patients, but infection was not confirmed and the patient's condition improved without treatment.

Transient Neonatal pustular melanosis may resemble various other skin rashes in the newborn, such as Erythema Toxicum Neonatorum (ETN), acne Neonatorum and eosinophilic pustular folliculitis, and it is essential to rule out systemic infection in patients presenting with these alterations. (20)

In ETN, in contrast to Transient Neonatal pustular melanosis the pustules are located in a background of erythematous skin and peripheral eosinophilia may be present. Histologically TNBM presents as subcorneal or intraepidermal pustules composed mainly of neutrophils. This finding helps to differentiate Transient Neonatal pustular melanosis from ETN, on which there is a predominance of eosinophils. (4)

Tzanck smear and CBC were also done in 38 more patients with severe skin rash, in whom these tests showed the characteristic neutrophilic content of the pustules and normal peripheral blood on differential blood count; this was in agreement with other studies. (4, 8, 9, 14, 16, 19, 22)

As the diagnosis of Transient Neonatal pustular melanosis was clinically evident in the rest of the subjects, skin biopsy and Tzanck smear were deemed unnecessary.

This could be because many of the mothers had drugs during pregnancy (63%), which may cause an allergic factor to be transferred to the baby through milk or placenta; this is not in agreement with other studies in which no association with maternal infections or exposure to toxic substances has been detected. (4, 9)

Although Transient Neonatal pustular melanosis appears to be a rare condition in newborns, its pathogenesis is still largely unknown. In our study, we noticed that the rash in subjects disappeared without treatment with no permanent sequelae. (1, 9)

## Conclusion

Transient Neonatal pustular melanosis is usually a self-limiting disease and without long term sequelae. More efforts are needed to raise awareness of this condition amongst health care professionals to avoid unnecessary investigations and treatment as it is sometimes misdiagnosed as bacterial infection.

## References

- 1- Jean L Bologna MD, Joseph L Jorizzo MD, et al. Vesiculobullous and Erosive Disease in the newborn. Third edition Dermatology ELSEVIER Saunders, 2012 ELSEVIER limited [www.elsevierhealth.com](http://www.elsevierhealth.com).
- 2- John Harper MD FRCP FRCPCH, Arnold Oranje MD PhD, et al, Common Transient Neonatal Dermatitis, Textbook of Pediatric Dermatology. Volume 1 Second edition, 2006 Blackwell Publishing Ltd. <http://www.blackwellpublishing.com>.
- 3- Jennifer Sorrell MD, Anne Elizabeth Laumann, MBChB, MRCP(UK), FAAD, et al editor. Transient Neonatal Pustular Melanosis. Medscape drugs, Diseases and procedures Reference.
- 4- Transient Neonatal Pustular Melanosis, ELSEVIER DOYMA, 2011 ELSEVIER Espana, S.l and AEDV. [www.elsevier.es/ad](http://www.elsevier.es/ad).
- 5- Tony Burns MB,BS,FRCP(EDIN), Stephen Breathnach MA, MB, BChir, MD, PhD, FRCP, et al, The Neonate, skin disorder in the neonate, Rook's Textbook of Dermatology VOLUME 1 SEVENTH EDITION, 1968,1972,1979,1986,1992,1998,2004 BY Blackwell Science Ltd, <http://www.blackwellpublishing.com>.
- 6- K.C Nischal, Uday Khopkar. An approach to the diagnosis of neutrophilic dermatoses: A histopathological perspective. 222 Indian J Dermatol Venereol Leprol/July-August 2007/ vol 73/ issue 4.
- 7- Dermatopathology Made Simple Pustular Reaction Pattern <http://dermatopathologymadesimple.blogspot.com/2012/09/pustules-on-histology.html>
- 8- M.C.G. Van Praag, MD., PhD., R.W.G. Van Rooij, et al. FETAL AND NEONATAL INVESTIGATIONS AND REPORTS, Diagnosis and Treatment of Pustular Disorder in the Neonate. Pediatric dermatology vol.14 no. 2 131-143. 1997.
- 9- Server Serdaroglu, MD, Bilgen Cakil, MD. Physiologic Skin Findings of Newborn. Blackwell Publ. 2004; 14:1-14.86. J Turk Acad Dermatol 2008; 2 (4): 82401r. <http://www.jtad.org/2008/4/jtad82401r.pdf>
- 10- Jayakar Thomas,. Neonatal dermatoses. PEDIATRIC DERMATOLOGY Year : 1999 | Volume : 65 | Issue : 2 | Page : 99-103 . IJDV : <http://www.ijdv1.com/article.asp?issn=0378-6323;year=1999;volume=65;issue=2;spage=99;epage=103;aulast=Thomas>
- 11- COMMON PAEDIATRIC SKIN CONDITIONS & BIRTHMARKS.2011 LA TUNISIE MEDICALE. [http://www.LA\\_TUNISIE\\_MEDICALE.com/article-medicale-tunisie.php?article=1459](http://www.LA_TUNISIE_MEDICALE.com/article-medicale-tunisie.php?article=1459) <http://learnpediatrics.com/body-systems/general-pediatrics/common-paediatric-skin-conditions-birthmarks/>
- 12- K. C. Nischal, Uday Khopkar, et al editor. An approach to the diagnosis of neutrophilic dermatoses: A histopathological perspective 222 Indian J Dermatol Venereol Leprol. July-August 2007|Vol 73|Issue 4. ([www.medknow.com](http://www.medknow.com)).
- 13- Gomathy Sethuraman, MD, Anthony J. Mancini, MD. Neonatal Skin Disorders and the Emergency Medicine Physician. [http://www.clinpedemergencymed.com/article/S1522-8401\(08\)00055-4/abstract](http://www.clinpedemergencymed.com/article/S1522-8401(08)00055-4/abstract). 2008 Elsevier Inc. All rights reserved.
- 14- Server Serdaroglu, MD, Bilgen Cakil, MD. Physiologic Skin Finding Of Newborn. Journal of the Academy of Dermatology. Eissn 1307-394x. Published : J Turk Acad Dermatol 3008; 2 (4): 82401 r, [www.jtad.org/2008/4/jtad82401r.pdf](http://www.jtad.org/2008/4/jtad82401r.pdf).
- 15- Benign vesicopustular eruptions in the neonate. Work done at University of Miami Miller School of Medicine - Miami (USA). Chief Resident of Pediatric Dermatology - University of Miami Miller School of Medicine - Miami (USA). Professor - Departments of Dermatology and Cutaneous Surgery and Pediatrics. Director - Division of

Pediatric Dermatology - University of Miami Miller School of Medicine - Miami (USA). *An Bras Dermatol.* 2006;(4):359-66.

\* <http://dermatology.med.miami.edu/pediatric-dermatology/>.

16- Ana Sayfa. Transient Neonatal Pustular Melanosis.

<http://www.belirtileritedavisi.com/transient-neonatal-pustular-melanosis.html>

17- Célia Kalil, MD; Zatti Fachinello, MD. et al Bullous Dermatoses in Childhood: Part I - *SKINmed.* 2007;6:73-78. <http://www.dermato.med.br/publicacoes/artigos/2007bollous1.htm>.

18- Wyre HW, Murphy MO. Transient neonatal pustular melanosis. *Arch Dermatol* 1979 Apr; 115(4) :458. Academy of Pediatrics. ©COPYRIGHT 2013 AMERICAN ACADEMY OF PEDIATRICS. ALL RIGHTS RESERVED. American Academy of Pediatrics. [https://www.pediatriccareonline.org/pco/ub/citation/434869/Transient\\_neonatal\\_pustular\\_melanosis?amod=aaapea&login=true&nfstatus=401&nftoken=00000000-0000-0000-0000-000000000000&nfstatusdescription=ERROR%3a+No+local+token](https://www.pediatriccareonline.org/pco/ub/citation/434869/Transient_neonatal_pustular_melanosis?amod=aaapea&login=true&nfstatus=401&nftoken=00000000-0000-0000-0000-000000000000&nfstatusdescription=ERROR%3a+No+local+token).

19- Mark R. Stephan, MD, Mary B. Kirby, MD, et al. COMMON NEWBORN DERMATOLOGIC CONDITIONS. <http://free-doc-lib.com/book/common-newborn-dermatologic-conditions-pediatric-1.pdf>. [http://www.familypractice.theclinics.com/article/S1522-5720\(03\)00066-7/abstract](http://www.familypractice.theclinics.com/article/S1522-5720(03)00066-7/abstract).

20- Faten Tinsa, Khadija Boussetta, et al. Congenital cutaneous candidiasis. *La tunisie Medicale* - 2010 ; Vol 88 ( n°011 ) : 844 - 846 . ©2011 LA TUNISIE MEDICALE. <http://www.latunisiemedicale.com/article-medicale-tunisie.php?article=1459>.

21- Jeffrey S Maly . A Parent's Guide To Skin Rashes and Dermatological Problems . Article Source: [http://EzineArticles.com/?expert=Jeffrey\\_S\\_Maly](http://EzineArticles.com/?expert=Jeffrey_S_Maly) .<http://ezinearticles.com/?A-Parents-Guide-To-Skin-Rashes-and-Dermatological-Problems&id=6076874> .

22- Rudolph, Colin D.; Rudolph, Abraham M.; et al. 14.2 NEONATAL DERMATOLOGY. Copyright ©2003 McGraw-Hill . <http://www.drugswell.com/winow/+Rudolph's%20Pediatrics/14.2%20NEONATAL%20DERMATOLOGY.htm>