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# CISPLATIN NEPHROTOXICITY AND HYDRATION PROTOCOLS

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# JSP

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Editor in Chief*

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# CISPLATIN NEPHROTOXICITY AND HYDRATION PROTOCOLS

Ahmed Usman, Heeranand Keswani, Suresh Nagdev, Ghulam Haider,  
Tehseen Khursheed, Anis Malik, Kasif Jafferri

## ABSTRACT

**Objective** *To evaluate the nephrotoxicity of cisplatin in cancer patients, using different protocols of hydration.*

**Study Design** *Randomized controlled trial.*

### Patients & Methods

*This study was conducted between 1st June to 30th November 2004. Ninety-nine patients with normal renal function were enrolled in the study and randomly assigned into the 3 study groups, each group having 33 patients. In group 1 hydration was done with saline (2 liter) alone, in group 2 with saline (2 liter) and furosemide (40mg) and in group 3 with saline (2 liter) and mannitol (100ml). All 3 group patients were given cisplatin infusion 100 mg/m<sup>2</sup> over 1 hour and the cycles repeated every 21-28 days. Twenty four hour creatinine clearance was measured before and after 6th day of the chemotherapy in all patients.*

### Results

*For the first cycle of chemotherapy the 24-hour urinary creatinine clearance before chemotherapy for saline group was 95.54+/- 15.27, for saline and furosemide group 98.43+/- 13.44 and for saline and mannitol group 97.45+/- 14.05 ml/min and after 6th day of cisplatin infusion was 77.4+/-14.59 for saline group, 86.06+/-11.9 for saline and furosemide group and 82.29+/- 13.64 for saline and mannitol group. The reduction in creatinine clearance was less with saline and furosemide group (12.6%) as compared to saline and mannitol group (15.6%) and saline alone (18.9%) which is statistically significant. Each patient in these 3 study groups received many courses of cisplatin and showed the similar pattern.*

**Conclusions** *Hydration with saline and furosemide is less nephrotoxic than other protocols with cisplatin infusion.*

**KEY WORDS** *Cisplatin, Nephrotoxic drugs, Cisplatin nephrotoxicity.*

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## INTRODUCTION

Cisplatin is a chemotherapeutic agent that has been used in the treatment of many malignancies including ovarian, germ-cell, small-cell lung, and head and neck malignancies. Different randomized studies have shown that adding cisplatin to the standard radiation therapy in

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different cancer reduces the risk of death by 30-50%<sup>1-6</sup> but nephrotoxicity still severely limits cisplatin use<sup>7</sup>. The mechanism by which cisplatin selectively kills the proximal tubule cells is still unknown. Recent study in mice and rats have hypothesized that cisplatin is activated in the proximal tubules of kidney into toxic metabolite through the action of gamma-glutamyl transpeptidase (GGT) and inhibition of GGT activity can reduce renal toxicity of cisplatin<sup>8</sup>. Within few hours of cisplatin infusion, the renal cisplatin concentration is much higher than in the liver and spleen<sup>9</sup> and this preferential renal binding is also the

suspected cause of renal toxicity. There is 33% reduction in renal blood flow and 78% reduction in glomerular filtration rate within 2 to 3 days of cisplatin infusion<sup>10</sup>. On cellular level cisplatin injures mitochondrial DNA, since mitochondria lacks the repair mechanism that exists in nuclear DNA<sup>11</sup>. These injuries lead to renal mitochondrial dysfunction<sup>12</sup> and decline in adenosine triphosphate production. Loss of function impairs the cellular sodium-potassium pump, which then reduces proximal tubular sodium and water absorption. As it is known that the largest concentration of renal mitochondria is in the proximal tubule<sup>13</sup> and this reduction in renal mitochondria causes a decreased proximal tubule re-absorption rate<sup>10</sup>. After cisplatin infusion in humans, the decrease in the glomerular filtration rate causes an increase in serum creatinine within 6 to 7 days. The serum creatinine levels remain elevated for 3 weeks<sup>14</sup>.

One recent study showed that low urine osmolarity could be a major determinant in the increase of cisplatin-induced nephrotoxicity and justify the widely used concurrent infusion of osmotically active substances during intravenous hydration<sup>15</sup>. In 1974 Higby DJ and friends done a phase-I study which revealed that cisplatin-induced nephrotoxicity is one of the most serious dose limiting factors<sup>16</sup>. However another study showed that hydration with saline and mannitol reduces nephrotoxicity<sup>14</sup>.

Studies involving furosemide diuresis used to decrease cisplatin-induced nephrotoxicity show conflicting results. A recent study showed that hydration with saline alone or saline with furosemide appear to be associated with less cisplatin nephrotoxicity than saline with mannitol<sup>17</sup>. We decided to conduct a study to evaluate the nephrotoxicity of cisplatin in cancer patients using different protocols of hydration.

## PATIENTS & METHODS

Adult male and female between the ages of 18 to 80 years were enrolled into this study. 100 mg/m<sup>2</sup> cisplatin was either given alone or in combination with 5-fluorouracil or paclitaxel or navelbine or gemcitabine to treat different cancers. The exclusion criteria were as follows: patient with poor performance status; diabetic and renal failure patient; serum creatinine >2 mg/dl; use of other nephrotoxic drugs (nonsteroidal anti-inflammatory drugs, aminoglycosides, amphotericin B, or cephalosporins) or drugs that falsely elevate serum creatinine (sulfonamides); previous history of abdominal radiation; or any health condition that would be exacerbated by fluid hydration (e.g. heart failure or pulmonary edema). Informed written consent was given by all enrolled patients. The study was conducted between 1st June 2004 to 30th November 2004.

A detailed history, physical examination, assessment of performance status were done in all enrolled patients and routine laboratory investigations along with , serum

creatinine and 24 hour creatinine clearance were sent to laboratory before each chemotherapy treatment. At each visit, the patient was instructed to collect urine over a single 24 hour period starting at 7 a.m. and ending at 7 a.m. the next morning. A special urine container was provided along with written instructions. Six days after cisplatin infusion, serum creatinine, 24 hour creatinine clearance, other standard laboratory investigations, and a physical examination were done in every patient.

All enrolled patients received chemotherapy with similar standard antiemetics and steroids (metoclopramide 40 mg i.v. and dexamethasone 20 mg i.v. for 30 min before chemotherapy). They were encouraged to increase their oral fluid intake before, during, and after cisplatin infusion. Patients who received paclitaxel, in combination to cisplatin, received cimetidine 400 mg i.v. and diphenhydramine 50 mg i.v. 30 min before chemotherapy. The patients were randomly assigned into the 3 study groups (table I) using a random allocation table. For safety reasons, any patient whose serum creatinine was 2 mg/dl or higher at any time during the study was excluded.

TYPE OF HYDRATION	BEFORE CISPLATIN INFUSION	DURING CISPLATIN INFUSION	AFTER CISPLATIN INFUSION
Saline	1000 ml NS in 2 h	Mix cisplatin in 500 ml NS	500 ml NS in 2 h
Saline + mannitol	1000 ml NS in 2 h	Mix cisplatin in 500 ml NS with 100 ml of mannitol	500 ml NS in 2 h
Saline + furosemide	1000 ml NS in 2 h. 40 mg furosemide 30 min before cisplatin	Mix cisplatin in 500 ml NS	500 ml NS in 2 h

NS: Normal saline

## RESULTS

During an interim analysis of 50 patients, the saline group was found to be slightly more nephrotoxic than other two groups. Ten patients were removed from study, 7 because of unable to collect the urine and 3 because of raised serum creatinine more than 2mg/dl after two courses of chemotherapy. The characteristics of the patients are shown in table II

The measured 24 hour creatinine clearance before and after six days of cisplatin infusion for the first chemotherapy course only is shown in fig. I. Ninety-nine patients gave 99 pairs of data points. For the first cycle of chemotherapy the 24-hour urinary creatinine clearance before chemotherapy for saline group was 95.54+/- 15.27, for saline and furosemide group 98.43+/- 13.44 and for saline and mannitol group 97.45+/- 14.05 ml/min and after 6th day of cisplatin infusion was 77.4+/-14.59

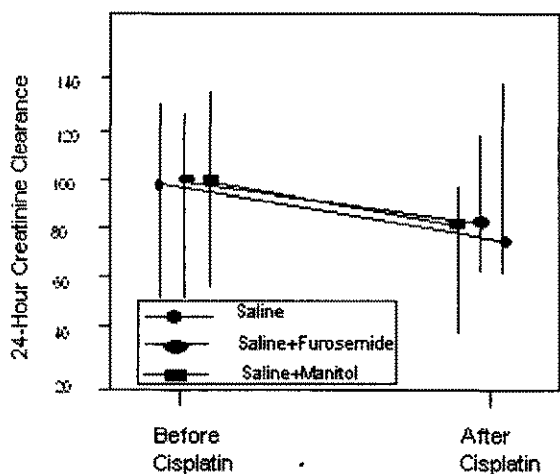
**TABLE II CHARACTERISTICS OF PATIENTS**

VARIABLE	SALINE	SALINE + FUROSEMIDE	SALINE + MANNITOL
AGE (YEARS) (MEAN±SD)	49.0±11.5	48.0±8.2	43.7±10.8
WEIGHT (KG) (MEAN±SD)	72.9±18.360.3±13.1	71.8±13.5	65.7±10.7
HEIGHT(INCH) (MEAN±SD)		61.3± 12.3	63.1±11.9
Male/Female	20/13	15/18	17/16
Number of patients Recruited	38	34	37
With incomplete data	4	3	3
Analyzed	33	33	33
Cisplatin alone	4	6	6
Cisplatin + 5-fluorouracil	12	13	15
Cisplatin + Gemcitabine	4	2	2
Cisplatin+ Navelbine	10	8	7
Cisplatin + paclitaxel	3	4	3

for saline group, 86.06±11.9 for saline and furosemide group and 82.29±13.64 for hydration and mannitol group. The reduction in creatinine clearance was less with saline and furosemide group (12.6%) as compared to saline and mannitol group (15.6%) and saline alone (18.9%) which is statistically very significant. Each patient in these 3 study groups received many courses of cisplatin and showed the similar pattern.

To confirm our study design of using 24 hour measured creatinine clearance instead of serum creatinine or calculated creatinine clearance, we determined the degree of correlation between serum creatinine and 24 hour creatinine clearance, and found a poor correlation (Pearson's correlation coefficient -0.52). The calculated 24 hour creatinine clearance using the Cockcroft-Gault method also tend to overestimate the measured 24 hour creatinine clearance (Pearson's correlation coefficient 0.62). Despite these discrepancies, a similar trend of declining creatinine clearance 6 days after cisplatin infusion continued when the glomerular filtration rate was estimated using serum creatinine or the Cockcroft-Gault method (table III, IV).

**FIGURE I MEASURED 24- H CREATININE CLEARANCE BEFORE AND AFTER CISPLATIN INFUSION. EACH POINT REPRESENTS THE MEAN (BARS ± SD)**



**TABLE III CALCULATED 24-H CREATININE CLEARANCE. DATA ARE PRESENTED AS MEAN ± SD**

HYDRATION TYPE	CREATININE CLEARANCE (ML/MIN) <sup>2</sup> BEFORE CISPLATIN INFUSION	CREATININE CLEARANCE (ML/MIN) <sup>2</sup> AFTER CISPLATIN INFUSION	% CHANGE	P VALUE (TWO-TAILED)
Saline	95.54±/ 15.27	77.4±/14.59	18.9	0.001
Saline + mannitol	97.45±/ 14.05	82.29±/13.64	15.6	0.001
Saline + furosemide	98.43±/ 13.44	86.06±/11.9	12.6	0.001

**TABLE IV CALCULATED SERUM CREATININE. DATA ARE PRESENTED AS MEAN ± SD**

HYDRATION TYPE	SERUM CREATININE (MG/DL) BEFORE CISPLATIN INFUSION	SERUM CREATININE (MG/DL) AFTER CISPLATIN INFUSION	P VALUE
Saline	0.84 +/- 0.13	0.93 +/- 0.3	0.03
Saline + mannitol	0.77 +/- 0.17	0.95 +/- 0.34	<0.002
Saline + furosemide	0.73 +/- 0.09	0.81 +/- 0.16	<0.001

**DISCUSSION**

Our data suggests that hydration with mannitol + saline and saline alone are associated with more nephrotoxicity than hydration with saline + furosemide. This basic knowledge is important, because cisplatin continues to be one of the most frequently used chemotherapy agents with dose-limiting nephrotoxicity. Our findings suggest a new paradigm that both furosemide and mannitol may decrease the cisplatin-related nephrotoxicity.

There are many ways of estimating glomerular filtration rate as an index of renal impairment: serum creatinine, inulin clearance, measured 24 hour creatinine clearance, calculated 24 hour clearance, and 51Cr-EDTA. But we selected 24-hr creatinine clearance as the most cost-effective compromise in measuring glomerular filtration rate. Serum creatinine, although easy to obtain, has been known to be elevated only in the late course of renal impairment and has been determined to be an inadequate measure of glomerular filtration rate<sup>18</sup>. Serum creatinine does not usually become abnormal until the glomerular filtration rate has been reduced by 50%. Inulin has the characteristics of an ideal glomerular filtration rate marker because it is freely filtered at the glomerulus but is not reabsorbed or secreted by the tubule. However, measurement clearance is difficult and clinically impractical. The 51Cr-EDTA clearance measurement has the highest correlation with glomerular filtration rate<sup>19</sup>, but it is costly and takes 1 to 3 hour per scan.

We used a total of 2 liter of normal saline for each

patient. This amount of hydration was taken from various Gynecologic Oncology Group studies. This approach was taken to simulate common clinical practice; therefore, the results of this study are applicable to clinical practice. In maintaining consistency to make our study applicable in general practice, we used serum creatinine in the inclusion and exclusion criteria and removal from the study. Many older studies of cisplatin nephrotoxicity have been criticized for using serum creatinine as end-points of the study, which prompted us to use measured creatinine clearance in the analysis of the study results.

Though the sample size of our study was relatively small as compared to other randomized trials, but we found statistically significant differences. A possible weakness of our study was dependence on the subjects to collect urine correctly. Intensive teaching and regular reinforcement of proper urine collection may improve compliance but may not absolutely remove the concern for accuracy.

We hope our results will encourage others to confirm our findings in a larger study and to evaluate other methods of reducing cisplatin toxicities (gastrointestinal toxicity, neurotoxicity, or ototoxicity) with saline + furosemide hydration compared with saline + mannitol or saline alone hydration.

#### REFERENCES:

1. Jay S C, Thomas F P, Arelene A.F, John J, Bruce H C, Scott B S et al. Postoperative Concurrent Radiotherapy and Chemotherapy for high risk squamous cell carcinoma of head and neck. *N Engl J Med* 2004; 350: 1937-44.
2. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler WC et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage 11B-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. *J Clin Oncol* 1999; 17:1339-48.
3. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* 1999; 340:1137-43.
4. Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med* 1999; 340:1154-61.
5. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999; 340:1144-53.
6. Peters WA, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS et al. Concurrent chemotherapy and pelvic radiation therapy as adjunctive therapy after radical surgery in high risk early stage carcinoma of the cervix. *J Clin Oncol* 2000; 18:1606-13.
7. Ozols RF, Young RC. High-dose cisplatin therapy in ovarian cancer. *Semin Oncol* 1985; 12:21-30.
8. Townsend DM, Deng M, Zhang L, Lapus MG, Hanigan MH et al. Metabolism of Cisplatin to a nephrotoxin in proximal tubule cells. *Am Soc Nephrol.* 2003; 14 :1-10.
9. Cornelison TL, Reed E et al. Nephrotoxicity and hydration management for cisplatin, carboplatin, and ormaplatin (review). *Gynecol Oncol* 1993; 50: 147-158.
10. Daugaard G, Abildgaard U, Larsen S et al. Functional and histopathological changes in dog kidneys after administration of cisplatin. *Renal Physiol* 1987; 10:54-64.
11. Clayton DA, Doda JN, Fiedberg ED et al. The absence of a pyrimidine dimer repair mechanism in mammalian mitochondria. *Proc Natl Acad Sci USA* 1974; 71:2777-81.
12. Gordon JA, Gattone VH. Mitochondrial alteration in cisplatin-induced acute renal failure. *Am J Physiol* 1986; 250: 991-98.
13. Tisher CA. Anatomy of the kidney. In: Brenner Rectors. *The kidney.* eds Saunders, Philadelphia, 1981; 28-35.
14. Hayes DM, Cvitkovic E, Goldberg RB, Scheiner E, Helson L, Krakoff IH et al. High dose cis platinum diammine chloride. *Cancer* 1977; 39:1372-81.
15. Polycarpe E, Arnould L, Schmitt E, Duvillard L, Ferrant E, Isambert N et al. Low urine osmolarity as a determinant of cisplatin-induced nephrotoxicity. *Int J Cancer.* 2004 10; 111:131-7.
16. Higby DJ, Wallace HJ, Albert DJ, Holland JF. Diaminodichloroplatinum: a phase-I study showing responses in testicular and other tumors. *Cancer* 1974; 33:1219-25.
17. Joseph T S, Joseph A L , Robert L C , Ilona S, Edward V H et al. Saline, mannitol, and furosemide hydration in acute cisplatin nephrotoxicity: a randomized trial. *Cancer Chemotherapy and Pharmacology* 2003; 52:13-24.
18. Levey AS, Perrone RD, Madias NE. Serum creatinine and renal function. *Annu Rev Med* 1988; 39:465-490.
19. Daugaard G, Rossing N, Rorth M. Effects of high dose cisplatin on glomerular function in the human kidney. *Cancer Chemother Pharmacol* 1988; 21: 163-67.



# SURGICAL MANAGEMENT OF RENAL TUMORS IN CHILDREN

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Nasir Saleem, Tariq Hussain, Salman Manzoor, Farhat Mirza

## ABSTRACT

**Purpose:** *To analyze case records of children with renal tumors.*

**Study Design:** *Case series.*

**Place & Duration of study:** *Surgical Unit B, National Institute of Child Health, Karachi during years 2004 - 2005.*

**Patients & Methods:** *Case records of all patients managed during the study period were reviewed for clinical presentation, investigations and surgical management. National Wilms' Tumor Study Group (NWTSG) and International Society of Pediatric Oncology (SIOP) protocols were used depending upon stage in cases of Wilms' tumor. Trucut biopsy was done for tissue diagnosis as proposed by UK Children's Cancer Study Group (UKCCSG). Touch imprints were also made. Surgical procedure was analyzed in terms of ease of dissection, tumor spillage and extent of excision.*

**Results:** *Twenty-one patients of renal tumors were managed in two years period. Nearly 60% of patients were less than 2 years of age. Majority (n 14) presented with abdominal mass. Few had complaints of abdominal pain. One patient an infant, presented with profuse hematuria. Trucut biopsy was done in 18 cases to have tissue diagnosis. Three patients underwent primary exploration. There were 17 cases of Wilms' tumor and in one case it was suspected on touch imprints. Fourteen patients of Wilms' tumor were given pre operative chemotherapy (SIOP protocol). Twelve of them were in stage III and IV. Nine out of this have undergone nephrectomy. Marked tumor regression in size of tumor was noted. The tumor also became firm. Only one tumor ruptured during excision. In one tumor with horse-shoe kidney, residual tumor left at margins of dissection. Three patients underwent primary nephrectomy. Two of these were in stage I and one in stage III (NWTSG protocol). Patient in stage III died in immediate post operative period because of hemorrhage. There was one case each of mesoblastic nephroma, cystic nephroma and rhabdoid tumor. In all these nephrectomy was done following trucut biopsy. Patient with rhabdoid tumor received pre operative chemotherapy. This tumor ruptured during surgery and gross spillage occurred.*

**Conclusion:** *Wilms' tumor was the most common pediatric renal tumor. Most of the patients were younger than the reported age and presented with advanced stage of disease. SIOP protocol found more appropriate in our group of patients.*

**Key words:** *Renal tumors, Wilms' tumor, Child, Chemotherapy protocol.*

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## INTRODUCTION

The overall incidence of malignancy in children is low in comparison with adult population. Leukemia and lymphoma are the most common tumors of childhood. The solid organ tumors are less common than hematological malignancies.<sup>1</sup> Kidney tumors represent 6.2% of malignant tumors in children. History, clinical course and radiological findings are necessary elements in the differential diagnosis of the various renal tumors.<sup>2</sup>

A broad spectrum of renal tumors occur in infants and children, ranging from the benign cystic nephroma to the extremely aggressive malignant rhabdoid tumor of the kidney. A thorough understanding of these tumors is crucial to the optimal diagnosis and management of children with renal masses. The most common malignant renal tumors of childhood are Wilms' tumor (WT), clear cell sarcoma of the kidney (CCSK), cellular mesoblastic nephroma (CMN), and rhabdoid tumor of the kidney (RTK).<sup>3,4</sup>

The literature from Pakistan lacks data on solid organ malignancy. Few studies are present in local literature on Wilms' tumor.<sup>5,6</sup> In this article we are sharing our experience of surgical approaches to the paediatric renal tumors.

## PATIENTS & METHODS

All patients with renal tumors admitted and managed in surgical unit B at National Institute of Child Health, Karachi during the years 2004 - 2005 were included. All patients with abdominal mass suspected of renal origin on clinical examination were subjected to ultrasound. Following confirmation of renal origin on ultrasound, CT scan was done. The purpose was to define the clinical stage and status of other kidney. General supportive care was started. Biopsy was taken under general anesthesia in physically fit patients otherwise local anesthesia was used. Trucut biopsy was the mainstay of acquiring tissue for biopsy as proposed by UK Children's Cancer Study Group (UKCCSG).<sup>7</sup> Touch imprints were made at the same time to have an immediate clue to the nature of the lesion.

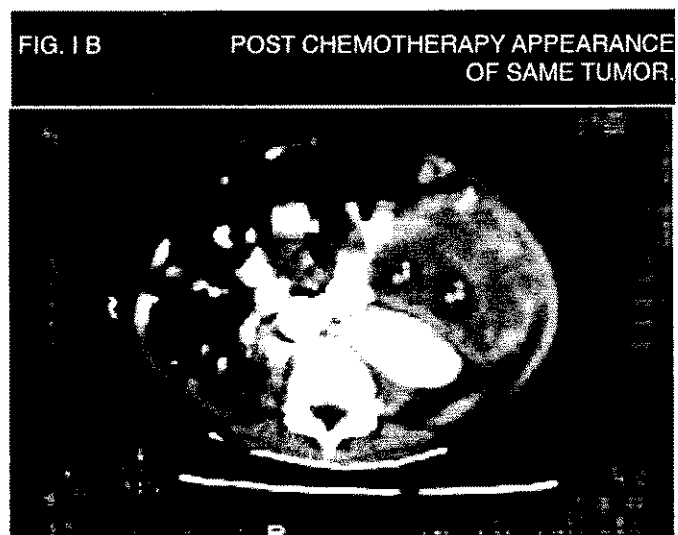
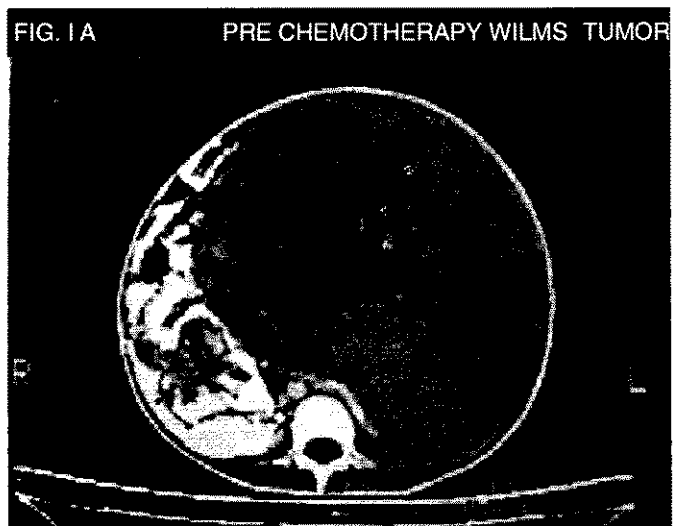
National Wilms' Tumor Study Group and International Society of Pediatric Oncology protocols were used but not very strictly.<sup>8,9</sup> All cases diagnosed as Wilms' tumor stage II and above were subjected to SIOP protocol. Following chemotherapy surgery was performed. During surgery ease of dissection, extent of excision and rupture of tumor were noted.

## RESULTS

In a two years period 21 patients with tumors of renal origin were managed. Six were infants, 10 between 1 - 2 years, 3 between 2 - 5 years and 2 above 5 years of age.

Fourteen patients presented with abdominal distension and mass was noted by the parents. Six patients had complaints of pain while one presented with profuse hematuria. Trucut biopsy was performed in 18 cases while three patients underwent primary nephrectomy. In 14 cases histopathologist made diagnosis of Wilms tumor. In one case rhabdoid variety of tumor was suggested and in two cases no definitive diagnosis made. In one case tissue was inadequate but there was suspicion of Wilms' tumor on touch imprints.

In total there were 18 cases of Wilms' tumor. Fourteen were diagnosed on trucut biopsy while three underwent primary nephrectomy. In one case there was suspicion of Wilms' tumor on radiology and touch imprints of the tumor cells, but as tissue was inadequate no conclusive diagnosis was made. This patient was lost to follow up. The stages of disease in this group is shown in table I. Fourteen patients received chemotherapy as per SIOP protocol and nine underwent nephrectomy thereafter. In 8 patients complete excision was performed while in one patient with horse-shoe kidney residual tumor was left at margins. The tumor sizes decreased to more than 50% and were firm in consistency (Fig. 1 A & B).



Dissection was not difficult as adhesions with surrounding tissues were easily separated. Only one tumor ruptured during removal. The spillage was local. Five patients are on chemotherapy. There were two patients of stage I who underwent primary nephrectomy. In one patient with stage III tumor, primary nephrectomy was attempted. It was not possible to remove the tumor and profuse hemorrhage occurred. The procedure was abandoned. This patient died in immediate post operative period.

In rest of the two out of three cases where trucut biopsy did not give definitive diagnosis, primary nephrectomy was performed. The final diagnosis in these cases was multicystic nephroma and mesoblastic nephroma. In multicystic nephroma chemotherapy was advised as tumor was huge crossing the midline and ruptured during surgery but parents refused. In patients with rhabdoid tumor chemotherapy was given initially. The size did not decrease appreciably. At surgery tumor was found densely adherent to surrounding viscera and ruptured. Gross spillage occurred. Tumor was ultimately removed. All patients with tumors were subsequently referred to oncologist (Table II).

		n=18
Stage I	2	
Stage II	3	
Stage III	12	
Stage IV	1	

N 17		
S.No	Tumor type	No of patients
1	Wilms tumor	17
2	Rhabdoid tumor	1
3	Multicystic nephroma	1
4	Mesoblastic nephroma	1

\*One patient was suspected of Wilms tumor on touch imprints

## DISCUSSION

Our data reveals that Wilms' tumor is the most common renal tumor of pediatric age group. It accounts for about 85% of all renal tumors as reported in literature. In our study its incidence is almost the same. As this study is of only 21 patients the results can not be generalized. More than 75% of our patients with Wilms' tumor were less than 2 years of age. This is different from what is reported in literature. The mean age mentioned in most of the series is 41.5 months<sup>10</sup>. The clinical presentation

did not differ from what is reported in literature. In one infant frank hematuria was the complaint. This patient on investigation found to have mass in the middle part of left kidney. As hematuria was non abating surgery was performed and nephrectomy done. It was found to be a case of Wilms' tumor with favorable histology.

Wilms' tumor is one of the successes of pediatric oncology, with an overall cure rate of over 85%. This is the result of multidisciplinary team approach. The two largest cooperative groups that have studied the optimum treatment for Wilms' tumor are the National Wilms' Tumor Study group in North America and the International Society of Pediatric Oncology, involving European and other countries. The National Wilms' Tumor Study group recommends primary surgery before any adjuvant treatment, whereas the International Society of Pediatric Oncology trials are based on the use of preoperative chemotherapy. The debate on primary chemotherapy versus primary nephrectomy appears to have been overcome, in the sense that the advantages and disadvantages of these two diverse methods have emerged from large and well-performed clinical trials<sup>11</sup>.

NWTSG protocols seem to be more aggressive and demanding especially in advanced stage of disease. In comparison tumor shrinkage following chemotherapy as in SIOP protocol, makes surgical excision easy and manageable. This is particularly true in our group of patients who present with advanced stage of disease and are malnourished and anemic. Anesthesia and surgery thus become hazardous. In our study more than 83% patients of Wilms' tumor were in stage III & IV at the time of presentation. In early SIOP protocol chemotherapy was started without histological prove. The diagnosis was based upon clinical and radiological grounds. It was found in subsequent analysis that chemotherapy was given unnecessarily in patients as they later found to have pathology other than Wilms' tumor<sup>12</sup>. UKCCSG recommends biopsy before start of chemotherapy. In our study we performed trucut biopsy in all cases. Our histopathologist was able to make diagnosis of malignancy on touch imprints, which was later proved at H&E staining of the specimen.

Surgery following chemotherapy was easy and tumor spillage occurred in only one case. In a case of rhabdoid tumor no significant change occurred following chemotherapy but tumor became firm although adhered to surrounding structure more densely. Bleeding was less and dissection thus facilitated in this case but gross spillage occurred at removal. The concern of change in stage of tumor following chemotherapy and histopathological features, are not found significant. In one of our patients with horse-shoe kidney and associated WAGR syndrome, following chemotherapy left kidney was removed. In this patient residual tumor found at margin of resection. No extension of tumor into vena cava found in any of the cases. One patient

had stage IV disease with pulmonary metastasis. In this patient following chemotherapy nephrectomy was performed. Pulmonary metastasis found on CT scan also disappeared.

In our study there was one case each of mesoblastic nephroma and multicystic nephroma. Both are rare pathologies<sup>13,14,15</sup>. In these cases trucut biopsy did not give diagnosis of pathology but ruled out Wilms' tumor. No chemotherapy was given to these patients and nephrectomy was done. Multicystic nephroma ruptured during the procedure.

In conclusion SIOP was the most suitable protocol in our group of patients as most of them were in advanced stage of disease at presentation with co morbid factors like anemia, malnutrition, RTI etc. Stehr et al also appreciated SIOP protocol in their clinical practice<sup>16</sup>. In a recent review on current therapy on Wilms' tumor published in *Oncologist*<sup>17</sup> the final recommendation are "In the absence of clear choice between up-front nephrectomy and preoperative chemotherapy, it is reasonable to base the timing of resection on factors such as tumor size, the patient's clinical condition, and the experience of the surgeon" and we agree with these guidelines.

#### REFERENCES:

- Breitfeld PP, Kreissman SG: Major tumors of childhood in *Pediatric Surgery* O'Neill JA, Rowe MI, Grosfeld JL, Fonkalsrud EW, Coran AG (Ed) Fifth Edition, Ch 23 Mosby – Year Book St Louis, Missouri 1998: 367- 78.
- Schenk JP, Gunther P, Schrader C, Ley S, Furtwangler R, Leuschner I, Edelhauser M, Graf N, Troger J. Childhood kidney tumors - the relevance of imaging. *Radiologe*. 2005;45:1112-23.
- Shamberger RC. Pediatric renal tumors. *Semin Surg Oncol*. 1999; 16:105-20
- Huang CC, Cutcliffe C, Coffin C, Sorensen PH, Beckwith JB, Perlman EJ. Classification of malignant pediatric renal tumors by gene expression. *Pediatr Blood Cancer*. 2006 19;46: 728-38
- Hanif G. Intra abdominal tumors in children. *J Coll Physicians Surg Pakistan*. 2004;14:478 – 80.
- Mahmood A, Ghafoor T, Badsha S. Wilms' tumor: Presentation and treatment. *J Coll Physicians Surg Pakistan*. 2004;14:142 – 45.
- Pritchard J, Imeson J, Barnes J et al. Results of the United Kingdom Children's Cancer Study Group first Wilms tumor study. *J Clin Oncol* 1995;13:124 - 33.
- Green DM, Breslow NE, Beckwith JB et al. Treatment with Nephrectomy only for small, stage I / favorable histology Wilms tumor: a report from the National Wilms Tumor Study Group. *J Clin Oncol* 2001;19:3719 – 724.
- Vujanic GM, Sandstedt B, Harms D et al. Revised International Society Pediatric Oncology (SIOP) working classification of renal tumors of childhood. *Med Pediatr Oncol*. 2002 38: 79-82.
- Gupta DK, Sharma S, Agarwal S, Carachi R. Saga of Wilms; tumor: Lessons learnt from the past. *J Indian Assoc Pediatr Surg*. 2005;10:217 – 228.
- Spreafico F, Bellani FF. Wilms tumor: past, present and (possibly) future. *Expert Rev Anticancer Ther*. 2006 ;6:249-58.
- De Kraker J, Graf N, van Tinteren H et al. Reduction of post operative chemotherapy in children with stage I intermediate risk and anaplastic Wilms tumor (SIOP 93-01trial). *Lancet* 2004;364:1229 – 35.
- Akhtar J, Qazi A, Aziz A. Congenital mesoblastic nephroma. *J Coll Physicians Surg Pakistan*. 1997;7:185-186.
- Singh S, Gupta R, Khurana N, Aggarwal SK, Mandal AK. Multicystic nephroma--report of two cases. *Indian J Pathol Microbiol*. 2004;47:520-23.
- Lenz MP, Warmann SW, Scheel-Walter HG, Schafer J, Wehrmann M, Hacker HW, A complicated case of bilateral cystic nephroma in a 16-month-old boy. *Fuchs J. Pediatr Surg Int*. 2005;21:1011-14.
- Stehr M, Deilmann K, Haas RJ, Dietz HG. Surgical complications in the treatment of Wilms' tumor *Eur J Pediatr Surg*. 2005;15:414-19..
- Metzger ML, Dome JS. Current therapy for Wilms tumor. *Oncologist* 2005;10:815 – 26.

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# NEONATAL UMBILICAL CORD CARE

Muhammad Aslam Memon

## ABSTRACT

**Objective** *To compare the effectiveness of various methods of umbilical cord care*

**Study Design** *Comparative study.*

**Place and Duration of Study** *From June 2004 to December 2004 at Hyderabad.*

## **Patients & Methods**

*Healthy full term, singleton new born with normal birth weight, whose cord was clamped with sterile plastic clips examined by author in the 1st 12 hours of life were included in the study.*

## **Results**

*Four hundred newborns were included in the study. Four groups of 100 each were made according to the cord care provided, group A- cord care using only natural drying, group B - 70% alcohol application, group C - polymyxin-bacitracin ointment and group D - bacitracin-neomycin powder application. The babies treated with alcohol had earlier cord detachment with least bacterial colonization with no exudate or granuloma formation.*

**Conclusions** *70% alcohol swab is a better choice for normal newborn umbilical care. The only drawback is it's cost and availability.*

**KEY WORDS** *Omphalitis, Neonate, Umbilical cord.*

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## INTRODUCTION

In developing countries umbilical cord infection constitutes a major cause of neonatal morbidity and poses a significant risk for mortality where outbreaks of cord infection continue to occur. Cord infection can be prevented through increased access to tetanus toxoid immunization during pregnancy, promoting clean cord care and reducing harmful cord applications and behaviors. Interventions introduced both in developed and developing countries to reduce exposure of cord to infectious pathogens include, clean cord cutting, hand washing before and after handling the baby, bathing of baby with antimicrobial agents and application of antimicrobial agents to the cord.<sup>1</sup>

The umbilical cord being composed of Wharton's jelly, is a well-known culture medium for growth of microbial agents, therefore it is not surprising that umbilical cord infection is the most common infection in neonatal period. The infection in umbilical cord may remain localized or may spread to abdominal wall, peritoneum, umbilical or portal vessel or liver. This may lead to bacteremia and septicemia. The portal vein phlebitis may result in extra hepatic portal hypertension.<sup>2</sup> Umbilical cord is the commonest site of neonatal tetanus. Not only contamination of the cord at birth but its subsequent soiling with infant's urine and stools and / or handling with unwashed hands also contribute to the infection. Therefore care of umbilical cord has always demanded special attention. Various methods ranging from application of animal dung, antimony powder to simple drying, methylated spirit, triple dye and antiseptic powder application, have been used with varying results. This study was conducted to assess the efficacy of various methods of umbilical cord care.

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## PATIENTS AND METHOD

Healthy singleton neonates born at full term, by normal vertex delivery, of either sex, examined within first 12 hours of life by the author were included in this study. Sterile plastic clip was applied to the umbilical cord at birth. Preterm, low birth weight babies, twins, large for gestational age and those with meconium staining or laceration of umbilical cord or where some material other than sterile plastic clip was applied, were excluded. The babies with clinical problem like birth asphyxia and malformations were also excluded. The babies included in this study were divided randomly into four groups.

1. Group A received simple dry cord care which consisted of spot cleaning of soiled skin in peri-umbilical area with soap and water, wiping it with dry cotton or cloth, allowing the area to air dry.
2. Group B received 70% alcohol swabbing thrice daily.
3. Group C had application of polymyxin-bacitracin skin ointment twice a day
4. Group D received application of neomycin-bacitracin powder thrice daily.

On 3<sup>rd</sup> day swab for culture and sensitivity were taken from the base of umbilicus. The day on which the umbilical stump shed was also recorded. Presence or absence of exudate and foul odour were noted. The same cord care was continued for 3 days after shedding. The baby was re-examined between 21 to 28 days for the formation of granuloma.

The acceptability was based on the ease to clean and use the antiseptics by the mother. The availability was based on presence of the particular antiseptics in 5 medicine outlet selected at random. Total cost of the product used per neonate was another criteria assessed.

## RESULTS

Four hundred babies were included in the study with 100 newborn assigned to each group. Table I and II show the results. The groups with 70% alcohol application and dry cord care had earlier cord detachment probably because of alcohol's own desiccating effect. The alcohol group had least bacterial colonization with no exudate, foul odour or granuloma formation. The maximum positive cultures were observed in natural drying group with staphylococcus aureus as predominant organism followed by E.coli. The granuloma formation was observed more in the polymyxin-bacitracin ointment group. The cost of alcohol swab (three swabs per day for 10 days, of alcohol prep-pad, containing 70% isopropyl alcohol cost Rs 1.00 per swab) and polymyxin-bacitracin ointment was almost same, but cost more than bacitracin-neomycin powder. The acceptability was maximum with alcohol swabs in terms of ease to apply, ease to clean but availability was main drawback being available at three out of five outlets.

## DISCUSSION

The care of umbilicus has long been a subject of discussion. What to use and what not to use has always created controversy. In some areas of this country people still apply animal dung and antimony powder. The more scientific application of triple dye, alcohol, chlorohexidine or antibiotic ointments have also been controversial. One million new born infant die every year by bacterial infection, which often have entered the body via umbilicus. Simply keeping the umbilical cord dry and clean are sufficient for healthy and term neonate in rich countries. Disinfectant does not offer any advantage. However cleaning the umbilical cord with disinfectant may reduce the risk of bacterial infection in babies in poor countries or in neonatal wards. Observational studies in poor countries indicate that life of numerous infants can be saved if pregnant women are vaccinated against tetanus and disinfectants are substituted for harmful cord care traditions.<sup>3</sup>

Cochrane systematic data review in 2004 concludes that good trials in low income setting are warranted. The review has not shown any advantage of antibacterial or antiseptic applications over simply keeping the cord clean and in this review no difference was demonstrated between cords treated with antiseptics compared with dry cord care or placebo.<sup>4</sup> A comparative trial of a triple dye-alcohol regime versus dry cord care revealed that infant with dry cord care were significantly more likely to be colonized with E.coli, staphylococcus and streptococcus as compared to triple dye / alcohol group. Community health worker also significantly more likely to observe exudate and foul odour among infants allocated to dry care group during home visits.<sup>5</sup>

Triple dye and 70% alcohol were also compared. Omphalitis was observed in 4.2% of triple dye group whereas in 10.7% of alcohol group. Triple dye group was 60% less likely to develop omphalitis as compared to 70% alcohol group. The mean duration for cord detachment were 13.6 and 11.5 days in triple dye and alcohol group respectively. It has been concluded that during an epidemic outbreak of omphalitis triple dye was the most appropriate and effective antiseptic to prevent omphalitis but delayed cord separation.<sup>6</sup>

Another study on alcohol versus natural drying showed that no newborn in either group developed cord infection. Bacterial colonization in two groups was equal but cord separation was significant statistically, being shorter with alcohol group. Mothers described similar comfort with cord care and relief with cord separation. Cost of alcohol drying while in the hospital was greater than that of natural drying.<sup>7</sup> Natural drying and 70% alcohol were also compared in preterm infants and analysis revealed that median cord detachment time was significantly shorter in natural drying group compared to alcohol group (13 versus 16 days) and there was no case of localized umbilical infection in either group.<sup>8</sup>

A study compared salicylic sugar powder with chlorhexidine and revealed that cord separation time was significantly lower in infants who were treated with salicylic sugar powder than those treated with chlorhexidine and one patient in chlorhexidine group also developed omphalitis. The rate of negative swab was also significantly high in salicylic sugar powder group.<sup>9</sup>

In Italy, eight different cord care regimens were studied in group of 1535 healthy neonates. The regimens studied were 70% alcohol, natural drying, salicylic sugar powder, triple dye, micronized green clay powder, colloid silver benzyl peroxide powder, neomycin bacitracin powder and 1% basic fuchsine. None of the newborns developed sepsis or died, with only sporadic case of omphalitis. With regard to cord separation time, best results were obtained with salicylic sugar powder, 5.6+/- 2.3 days and micronized green clay powder 6.7+/- 2.2 days. Both forms of treatment proved to be more effective than others. With salicylic sugar powder the rate of positive umbilical swab was also low and significantly higher only than the results obtained with neomycin-bacitracin regimen.<sup>10</sup>

Double blind comparative study using 80% alcohol with or without chlorhexidine in 100 neonates in National Tokyo Medical Center was carried out. It showed that there was least contamination with staphylococcus aureus in chlorhexidine group (25%) than with alcohol alone (57%) and hence recommended that for daily care of neonatal umbilicus, disinfectant using 80% ethanol containing chlorhexidine was more effective than ethanol alone.<sup>11</sup>

In a comparative study of 4 methods of umbilical antisepsis using 70% alcohol, mercurochrome, a solution of alcohol and mercurochrome and 1% chlorhexidine in 311 normal neonates, the authors reported that umbilical cord colonization was significantly reduced with chlorhexidine as compared with 3 other methods used but it took longer time to shed off (14 days) as opposed to mean of 8 days with other methods.<sup>12</sup> Another comparison was made between alcohol and rikospray in terms of separation time of umbilical cord. The time of cord separation and post fall umbilical complications in two groups, was similar.<sup>13</sup>

From above discussion it is clear that keeping the umbilicus clean is the mainstay in preventing infection no matter whatever method is used. In our study alcohol treatment found to be superior to other methods. It enhances cord separation with least bacterial colonization. Alcohol swabs were easy to apply and did not require any cleaning. The mothers found lot of difficulty in keeping the cord clean with dry cord care method. The application of ointment and antiseptic powder were messy and difficult to clean both for mothers and nursing staff.

TABLE I COMPARISON BETWEEN THE GROUPS

Total No 400						
No.	Group	A	B	C	D	TOTAL
1	Number	100	100	100	100	400
2	Sex a: Male	40	53	38	43	174
	b: Female	60	47	62	57	226
3	Day of cord detachment	10+/- 1.5	10+/-1.5	12+/-2	12+/-2	
4	3rd day culture	29%	15%	27%	21%	20.50%
	a: Staph.aureus	22%	10%	15%	12%	12.20%
	b: E.Coli	7%	5%	12%	9%	8.20%
5	Exudate formation	6%	0%	8%	3%	4.20%
6	Foul Odour	2%	0%	2%	2%	1.50%
7	Granuloma Formation	0%	0%	1%	0%	0.20%

TABLE II ACCEPTABILITY

Group	A	B	C	D
Easy to apply	100%	100%	100%	100%
Easy to Clean	15%	100%	60%	60%
Availability	100%	60%	100%	100%
Cost in Rupees	Nil	30.00	32.98	20.63

## REFERENCES

- Mullary LC, Darmstadt GL, Tielsch JM. Role of antimicrobial application to the umbilical cord in neonates to prevent bacterial colonization and infection. A review of evidence. *J Pediatr Infect Dis.* 2003; 22: 996-1002.
- Stoll.BJ, Kliegman RM. The umbilicus in Behrman RE, Kliegman R.M, Jenson H.B (Ed s) *Nelson Textbook of Pediatrics*, 17<sup>th</sup> Edition, Philadelphia ,W.B Saunders 2004:609.
- Zupan J, Garner P. A Cochrane systematic review on umbilical cord care and prevention of infection. *Lakartidningen* 2002;99:1563-6
- Zupan J, Garner P, Omari AA. Cochrane data base systemic review on topical umbilical cord care at birth. *Cochrane Database Systemic review.* 2004: CD :001057.
- Janssen PA, Selwood BL, Dobson SR, Peacock D, Thiessen PN. To dye or not to dye: A randomized clinical trial of a triple dye/alcohol regime versus dry cord care. *Pediatrics* 2003;112:15-20.

6. Panyauvahikrai S, Danchaivijitr S, Vantanasiri C, Trakulsomboon S, Kolatat T, Dhiraputra C, Poomsuwan V, Srihapal N. Antiseptic for preventing omphalitis. *J Med Assoc Thai.* 2002;85: 229-34
7. Dore S, Buchan D, Coulas S, Hamber L, Stewart M, Cowan D, Jamieson L. Alcohol versus natural drying for new born cord care. *J Obstet Gynaecol Neonatol Nurs.* 1998;27: 621-7
8. Evens K, George J, Augst D, Schweig L. Does umbilical cord care in preterm infants influence cord bacterial colonization or detachment. *J Perinatol* 2004;24 100:4
9. Pezzati M, Rossi S, Tronchin M, Dani C, Fillipi L, Rubaltelli FF. Umbilical cord care, in premature infants; the effect of two different cord care regimen on cord separation time and other outcome. *Pediatrics* 2003;112: 275-77.
10. Pezzati M, Biagioli EC, Martelli E, Gambi B, Biagiotti R, Rubaltelli FF. Umbilical cord care, the effect of eight different cord care regimen on cord separation time and other outcome. *Biol Neonatol.* 2002;81: 38-44
11. Oishi T, Iwata S, Nonoyama M, Tsuji A, Sunakawa K. Double blind comparative study on care of neonatal umbilical cord using 80% ethanol with or without chlorohexidine. *J Hosp Infect.* 2004;58: 37-7
12. Perapoch LJ, Salcedo AS, Gallart CA, Peguero MG, Cesellas CM, Barroso PC, Fernandez PF, Rodriguz GV. Umbilical colonization in normal new born ; a comparative study of 4 methods for umbilical antiseptis. *Pediatrics.* 1993;39:195-8
13. Noar N, Merlab P, Litwin A, Wiepunksy E. Time of separation of umbilical cord A comparative study of treatment with alcohol and Rikospray. *J Obstet Gynecol Repord Biol.* 1989; 32:89-93.



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# A STUDY OF DIABETIC FOOT SYNDROME

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## ABSTRACT

**Objective** *This study was carried out to determine the number and predisposing factor of foot infection in the adult onset diabetes mellitus.*

**Study Design** *An observational study.*

**Place and Duration of Study** *The study was carried out at PAF Hospital Islamabad, from June 2003 to June 2005.*

**Patients & Methods** *A total of 130 patients with adult onset diabetes mellitus were included in this study. The population was mixed. Clinical profile and investigations were recorded. Patients were managed as indoor cases. Plain insulin was used to control the diabetes. Broad-spectrum antibiotics and serial debridments, where required, were carried out.*

**Results** *A total of 18.5% of the hospitalized diabetic population was due to foot infection. Males were affected 1.5 times more than the females. The disease was bilateral in 4% cases. Poor control of diabetes, bad foot hygiene, peripheral neuropathy, trauma, ingrowing toenails, callosities and corns were implicated as predisposing factors in majority of cases.*

**Conclusions** *Foot infection in diabetics is a common occurrence and both sexes are involved though males more commonly than females. Majority of the patients were elderly and have poor knowledge and insight of their disease.*

**KEY WORDS** *Diabetic foot, Adult onset diabetes mellitus, Foot infections*

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## INTRODUCTION

The diabetics tend to have increased foot pressures, and this can be demonstrated in them even with early sensory neuropathy<sup>1</sup>. Most of the diabetic ulcerations occur at the areas of maximum pressure, the metatarsal heads; a callus may cause 18,600 kilograms of excess plantar pressure per day<sup>2</sup>. Foot problems are common in the population at large, however, the diabetics are especially vulnerable because of increased pressures and the complications of arteriosclerosis obliterans and peripheral neuropathy. The combination of these factors compounded by infection can lead to gangrene and amputation.

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Although advances in the medical treatment of diabetes mellitus have resulted in a dramatic decrease in the life-threatening metabolic disorders, but, this has not been paralleled by a reduction in the main diabetic complications of retinopathy, nephropathy, vasculopathy and foot disease, which are presenting with increasing frequency. In the lower limb the group of symptoms and signs involving neuropathies, angiopathies and infective lesions constitute the entity known as the diabetic foot syndrome<sup>3</sup>.

The increase in diabetic complications is likely to continue as: The prevalence of diabetes is approximately 1.5% with 80% presenting over the age of 40 and duration of diabetes is associated with onset of complications, and after 10 years most diabetic feet show some changes of

neuropathy or angiopathy. The diabetic complications are progressive with increasing and recurrent susceptibility to foot breakdown.

Thus the diabetic who is most likely to develop a foot lesion is over age 40. Of all diabetic population, 15-20% has foot problems<sup>4</sup>, and 15% will develop a foot ulcer during their lifetime<sup>5</sup>. Most of these are the result of peripheral neuropathy and the insensate foot. Peripheral neuropathy is extremely common in the diabetic with the incidence gradually increasing with age and duration. After 20 years of diabetes 42% of diabetics have evidence of peripheral neuropathy<sup>6</sup>. 8% diabetics are having angiopathy at the time of diagnosis, 15% after 10 years, and 45% after 20 years<sup>7</sup>. Of diabetics, 20% will enter the hospital because of foot problems<sup>8</sup>. Of these patients, 30% have symptomatic angiopathy and 7% will require vascular surgery or amputation. The overall number of amputations performed is greater in type II (adult onset) diabetics than in type I. This is largely because type II diabetics are older and greater in number.

The purpose of present study was to find out the number and predisposing factors of diabetic foot syndrome in our setup.

#### PATIENTS AND METHODS

The study was carried out over a period of 24 months. A total of 130 patients with diabetes mellitus were admitted to Pakistan Air Force Hospital Islamabad, over this period with various problems. Out of these twenty-four diabetics with diabetes of adult onset having foot infection were managed in the department of surgery as indoor cases. The histories and the findings of examination and investigations were entered on a performa.

The diabetes was monitored by serial blood glucose and urine glucose levels. All previous treatment of diabetes mellitus was discontinued and the patients were put on plain insulin, which was monitored by serial blood glucose estimations. Swabs and tissue for culture and sensitivity were taken from the infected part and broad-spectrum antibiotics started. Radiology of the foot was done in all cases to determine the involvement or otherwise of bone and to see the evidence of gas in the tissue planes. The doppler studies to assess the vascularity could not be performed due to lack of this facility in the hospital.

#### RESULTS

Out of all the diabetics admitted, 24 (18.5%) had foot infection, thus forming a large proportion of total diabetic hospitalizations. Out of these 24 diabetic patients, 15 (62.5 %) were males and 9 (37.5%) females. The age ranged from 44 to 88 years. In 23 (96%) only one foot was infected while in 1(4%) the disease was bilateral. Twenty Two (91.66%) patients were known diabetics and 2(8.34%) patients, on investigations were found to be diabetics. Four (16.66%) patients at the time of

admission were on insulin therapy, 14 (58.33%) were using oral hypoglycemic agents, 4 (16.67%) of the cases were being treated by diet alone and 2 (8.34%) cases were on no treatment. Seven (29%) cases had evidence of poor foot hygiene whereas in nine (37.5%) peripheral neuropathy was incriminated as a predisposing factor. Other factors attributed were: 2 (8.33%) penetrating trauma, 2 (8.33%) in growing toenails and 1 (4.16%) corns. In 3 (12.5%) cases no predisposing factor could be found. In 11 (46%) patients the infection was confined to the plantar aspect of the foot, in 3 (12.5%) dorsal surface of the foot was involved alone, while 2 patients (8.3%) had involvement of both the plantar as well as dorsal surfaces of the foot. The forefoot was found to be involved in 6 (25%) patients.

#### DISCUSSION

Diabetes mellitus is a common illness and foot infections are amongst the commonest reasons for hospitalization of the diabetics. Once the infection is established in the foot of a diabetic patient, it may mean loss of many working days, disfiguring surgery, permanent disability and a lower quality of life apart from the high costs incurred on the treatment<sup>9</sup>. Therefore, to understand and prevent the infections in diabetics, recognition of factors that predispose to foot infection, are of great importance if one has to identify the individuals at high risk and be successful in the management of diabetes mellitus, and its sequelae<sup>10</sup>.

In our study we have found a sex predilection for the males probably because the male works outdoors more as compared to the female and his foot is thus more prone to trauma as well as other detrimental factors effecting the foot. In this study 58% of the patients were between the ages of 51 and 60 years, and a total of 79% came into the bracket of elderly being above the age of 50 years. The reason of this high incidence amongst the older age group is that the adult onset diabetes starts around the age of 40 and it takes a further few years for the disease to tax the foot by peripheral neuropathy and angiopathy.

Peripheral neuropathy followed by poor hygiene were found to be the commonest cause of pedal sepsis in our set up. Peripheral neuropathy was also the leading cause of foot sepsis noted in other studies as well<sup>11, 12, 13</sup>. With the onset of peripheral neuropathy in diabetics the foot care becomes all the more important and the physicians should be more vigilant and careful in examining and guiding the patient in the care of their feet. Foot infections in diabetics are polymicrobial. Both aerobes and anaerobes as well as gram positive and gram-negative organisms were cultured from the infected materials. Most of the infections affect the plantar surface as this is the part of the foot most taxed by the ambulatory forces and is most prone to ischaemia and trauma. Timely debridment can save the foot from a most feared amputation--the incidence of which, however, remains

high in diabetic s foot infection. Prevention is, therefore, of utmost importance in the successful management of diabetes like many other major health problems. Not only an effective control of diabetes is required, but, repeated patient education in foot care, regular evaluation of foot as well as footwear and careful nail trimming is mandatory in the prevention and prophylactic care of the diabetic foot<sup>14</sup>.

Foot salvage and restoration of function should, however, be the prime aim in the management of diabetics with foot infection. It is therefore, most desirable that a stage beyond salvage is not reached. For this the physicians managing diabetes mellitus play an important role by referring the diabetics, having foot infection, to the surgeon as early as possible as the delay until the infection has set well in the deeper tissues may cost the patient his limb or even life

#### REFERENCES

1. Boulton, AJM. Abnormalities of foot pressure in early diabetic neuropathy. *Diabetic Med* 1987; 4.
2. Pataky Z, Goly A, Faravel L. The impact of callosities on the magnitude and duration of plantar pressure in patients with diabetes mellitus. *Diabetes Metab* 2002; 28: 356-61.
3. Shilling F. Foot care in patients with diabetes. *Nurs Stand.* 2003;17:19-25.
4. Bal A. Diabetic foot magnitude of the problem. *J Indian Med Assoc.*, 2002; 100: 155-7.
5. Palumbo P, J Melton LJ. Peripheral vascular disease and diabetes. In *Diabetes in America: Diabetes data compiled in 1984*. Washington, DC, US Government Printing Office, 1985.
6. O'Brien, I.A.D. Corral R.J.M. Epidemiology of diabetes and its complications. *N Engl J Med* 1988; 318, 1619.
7. Melton L. Incidence and prevalence of clinical peripheral vascular disease in a population-based cohort of diabetic patients. *Diabetes Care.* 1980; 3:650.
8. Block P. The diabetic foot ulcer, a complex problem with a simple treatment approach. *Milit Med* 1981; 146: 644.
9. Thompson C, McWilliams T. Importance of diabetic foot admissions at Meddlemore Hospital. *N Z Med J* 1993; 106: 178-80.
10. Adler A. Risk factors for diabetic neuropathy and foot ulceration. *Curr Diab Rep* 2001; 1: 202-7.
11. Khan AZ, Gondal K.M. Four years experience of Management of diabetic foot. Department of Surgery Mayo Hospital Lahore. *Pakistan J Surg.* 1995; 11, 161-164.
12. Ramani A, Kundaji GN. Aetiology of diabetic foot ulceration. Department of Medicine, Kosturba Medical College, Manipal, India. 1990; 843-5.
13. Sosenko J. The epidemiology of neuropathic foot ulcers in individuals with diabetes. *Curr Diab Rep* 2002; 2: 477-81.
14. Levin ME. Diabetic foot ulcers, Pathogenesis and Management. *J Em. Nurs* 1993; 20: 191-8.

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All authors worked in Field Hospital, Lipa, Kashmir during the study period.

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# CHRONIC SUPPURATIVE OTITIS MEDIA: DISEASE PATTERN AND DRUG SENSITIVITY

Syed Mosaddaqa Iqbal, Iqbal Hussain Udaipurwala, Ahmed Hasan, Mohammad Shafiq, Shoaib Mughal.

## ABSTRACT

**Objective** *To identify the frequency of bacterial isolates associated with chronic suppurative otitis media (CSOM) and to determine their antibiotic sensitivity pattern.*

**Design** *Descriptive study.*

**Place and Duration of Study** *Department of E.N.T, Jinnah Medical & Dental College Hospital, Korangi Karachi, from April 2003 to June 2005.*

**Patients & Methods** *Two hundred patients of CSOM were included in this study. Ear swabs were taken from these patients and cultured on chocolate and blood agar. Antibiotic sensitivity was determined by disc diffusion method using Muller Hinton agar. Biochemical tests were used in identifying gram-negative bacteria.*

**Results** *From 200 ear swabs different micro-organisms were isolated. The bacteria isolated were Pseudomonas aeruginosa in 83 cases, Staphylococcus aureus in 38 patients, Proteus mirabilis in 36, Klebsiella pneumoniae in 21, Escherichia coli in 8, beta haemolytic Streptococcus in 10 and Serratia species in 4 patients. Most of the bacterial isolates were resistant to common antibiotics but they were sensitive to ofloxacin (92.2%), ciprofloxacin 92.2%), amikacin (90%), gentamycin (88.4%), ceftazidime (86.4), ceftriaxone (70.4%), polymyxin B (70%), amoxicillin clav.(40%), ampicillin(10%), cephradine(10%), erythromycin(6%).*

**Conclusions** *In CSOM, high rate of multiple drug resistance specially to frequently used antibiotics has risen.*

**KEY WORDS** *Chronic suppurative otitis media, Bacterial isolates, Antibiotics.*

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## INTRODUCTION

Chronic suppurative otitis media is the chronic inflammation of the middle ear cleft mucosa for more than eight weeks duration. It can present at any age with ear discharge, deafness and perforated tympanic membrane.<sup>1</sup> It may be secondary to acute otitis media as a result of inadequate treatment, drug resistance, high virulence or polymicrobial infection. Active CSOM

accounts for a major proportion of the clinical work load. It can result in serious intracranial complications such as meningitis, focal encephalitis and intracranial (brain) abscess.<sup>2</sup> Thus, it can cause serious handicap in terms of language skills and mental development, specially in children.<sup>3</sup>

The wide range of micro-organisms, both aerobic and anaerobic, are involved in CSOM.<sup>4,5</sup> Infection may be polymicrobial but in majority of the cases gram negative aerobes are isolated.<sup>6</sup> In these patients multiple factors are responsible for drug resistance.<sup>7</sup> Lack of awareness

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about health care and limited medical facilities, indiscriminate use of antibiotics like self medication, improper selection of antibiotics and sub standard dosage are few of them. This study was conducted to find out the type of organisms and their antibiotics sensitivity pattern in CSOM.

### PATIENTS AND METHODS

This study was conducted in the out patient clinic of E.N.T department at Jinnah Medical & Dental College Hospital, Korangi, Karachi, in collaboration with our pathological laboratory for culture and sensitivity, between April 2003 and June 2005. Two hundred patients with persistent ear discharge of more than eight weeks duration were selected for this study. Cases of CSOM in pregnant and lactating mothers, cholesteatoma, marginal perforation or dry perforation and patients not coming for follow up, were excluded from this study.

All the patients had purulent discharge and perforated tympanic membrane. A detailed history and E.N.T examination were done. Two hundred specimens were cultured on chocolate agar using blood agar base and incubated for 24 hours at 37c in Co<sub>2</sub> rich surrounding. Antibiotic sensitivity of isolated micro-organisms was determined by the disc diffusion method using Muller Hinton agar by first making a McFarland standard of 0.5% suspension turbidity and incubation for 24 hours at 37c. The disc diffusion method of grading zone of inhibition was also used.

### RESULTS

In majority of the patients the micro-organism was *Pseudomonas aeruginosa* (83), followed in the descending order of frequency by *Staphylococcus aureus* (38), *Proteus mirabilis* (36), *Klebsiella* (21), beta haemolytic streptococcus (10), *Escherichia coli* (8), *Serratia* species (4). The antibiotic sensitivity of the organisms is given in table I.

S.NO.	ANTIBIOTICS	% OF EFFECTIVENESS
1	Ofloxacin	92.2
2	Ciprofloxacin	92.2
3	Amikacin	90.0
4	Gentamicin	88.4
5	Ceftazidime	86.4
6	Ceftriaxone	70.4
7	Polymyxin	70.0
8	Amoxicillin Clav	40.0
9	Ampicillin	10.0
10	Erythromycin	6.0

### DISCUSSION

Isolation of causative micro-organisms and selection of appropriate antibiotics are of paramount importance in the medical management of CSOM. It is a persistent and insidious disease that often leads to destructive changes and irreversible squeale.<sup>8</sup> The common antibiotics such as penicillin, erythromycin and others that have been used for long period, have now become ineffective due to many reasons.<sup>9</sup> In every day practice abuse of antibiotics is a routine as they are used in cases where they not even required, thus resulting in emergence of resistant organisms. In indirect pathogenesis the commensals help the accompanying pathogenic bacteria by increasing beta lactamase.<sup>10</sup> These enzymes also inhibit the activity of certain antibiotics.

Due to massive clinical work load doctors do not consider worth doing aural pus swab for culture of microbial flora and selection of appropriate antibiotics. This study was carried out for the identification of micro-organisms of CSOM in our setup and to stress the importance of culture and sensitivity in the management of CSOM. The common organisms isolated in this study in descending order of frequency were *pseudomonas aeruginosa* and *staphylococcus aureus*. This study is almost in accordance with the previous studies. Brookes from USA also found the highest incidence of *pseudomonas aeruginosa* followed by *staphylococcus aureus* and *klebsiella pneumoniae*. Aslam et al<sup>11</sup>, Manzoor et al<sup>12</sup>, Javed et al<sup>13</sup> and Yang et al<sup>14</sup> also described the *pseudomonas aeruginosa* followed by *staphylococcus aureus* and *proteus mirabilis* as the common organism. We found mono-bacterial isolate in 88% and two bacterial species in 12% of the cases. Aslam et al reported single strain in 86.88% and more than one in 13.12%. Javed et al found single strain in 92% and two species in 8%.

Regarding susceptibility to antimicrobials we found that most effective antibiotics were quinolones (ofloxacin and ciprofloxacin), aminoglycosides (amikacin and gentamicin) and 3<sup>rd</sup> generation cephalosporins (ceftazidime, ceftriaxone). Most of the commonly used antibiotics like penicillin, amoxicillin clavulanic acid, cephadrine, doxycyclines found less effective, suggesting inappropriate use for a longer period thus organisms become resistant to them.

Thus we can suggest that in the conservative (medical) management of CSOM the clinician should choose a group of antibiotics which is specially effective against *pseudomonas aeruginosa*, *staphylococcus aureus* and *proteus mirabilis*. The high rate of multiple drug resistance as well as high levels of resistance to individual antibiotics is a cause of concern. Culture and sensitivity remains time tested investigation of choice for better medical treatment of CSOM. It has multiple advantages like, preventing development of resistant strains of organisms, minimizing complications and total cost of treatment. Thus we recommend this cost

effective, easily acceptable and effective investigation to get the best possible results of the medical management of CSOM.

**REFERENCES**

<p>1. Senturia BH, Bluestone CD, Klein JD. Definition and classification of the otitis media. <i>Am J Otol Rhinol Laryngol</i> 1980; 89: 3-4.</p> <p>2. Bernman S. Otitis media in developing countries. <i>Pediatrics</i> 1995; 96: 126-31.</p> <p>3. Cuotonen M, Uhar M, Aitoza L, Lukkaroinen AM, Luotonen J, Uharic M. Recurrent otitis media during infancy and linguistic skills at the age of 9 years. <i>Pediatr Infect Dis J</i> 1996; 15: 854-8.</p> <p>4. Brook L. Prevalence of Beta lactamase producing bacteria in CSOM. <i>Am J Dis Child</i> 1985; 139: 280-283.</p> <p>5. Constable I, Butler I. Microbial flora in CSOM. <i>J Infection</i>. 1982; 5: 57-60.</p> <p>6. Fairbanks DNF. Antimicrobial therapy for CSOM. <i>Ann Otol Rhinol Laryngol</i> 1981; 90: 58-62.</p>	<p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p>	<p>Browning G. Medical management of CSOM. <i>Clinical Otolaryngol</i> 1984; 9:141-144.</p> <p>Fiss D M, Dagan R, Meidan N, Leiberman A. Aerobic bacteriology of CSOM with cholestaetoma in children. <i>Ann Otol Rhinol Laryngol</i> 1992;101: 866-869.</p> <p>Fairbanks DNF. Antimicrobial therapy for CSOM. <i>Ann Otol Rhinol Laryngol</i>. 1981;90:58-62.</p> <p>Karma P, Jokipii I, Ojala K. Bacteriology of the CSOM. <i>Acta Otolaryngologica</i>. 1978; 86: 110-114.</p> <p>Aslam M, Hassan S.M, Parbenn N, Khan JA. Bacteriology in the chronic discharging ears in Aligarh, India, <i>Pak J Otolaryngol</i> 1998; 14:33-34.</p> <p>Ahmad M, Amjad M, Hameed A. Microflora in CSOM. <i>Specialists</i>.1995;12:19-22.</p> <p>Javed MF, Kharal SA, Rafi T. Selection of antibiotic in CSOM. <i>Pakistan J Otolaryngol</i>.1999;15: 7-9.</p> <p>Yang Y, Gong S, Liu Y. Clinical investigation of bacteriology of chronic suppurative otitis media;15 12:550-2.</p>
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# LUPUS NEPHRITIS: CLINICOPATHOLOGICAL CORRELATION

Manan Junejo

## ABSTRACT

**Objective** *To analyze clinicopathological correlation in lupus nephritis (LN).*

**Design** *Analytical study*

**Place and Duration of Study** *Two years (January 2002 to December, 2004) study conducted at the Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi.*

**Patients & Methods** *Thirty patients of both sexes between ages of 15 – 70 years, fulfilling criteria of primary SLE and with renal impairment were included in the study. Various investigations like complete blood picture, blood urea nitrogen (BUN), serum creatinine, 24 hours urinary protein, creatinine clearance, ANA, double stranded DNA (Anti Ds DNA), ultrasound of kidneys were carried out. Ultrasound guided renal biopsy was done in all cases.*

**Results** *Proteinuria was found in all 30 cases, nephrotic syndrome in 18 (60%) patients, oliguria in 17 (56.60%), microscopic hematuria in 20 (66.60%) and hypertension in 21 (70%) cases. Various clinical features of SLE including arthritis in 20 (66%), arthralgia 26 (86.60%), serositis 7 (23%) and anemia in 20 (66.6%) cases. Renal biopsy results were classified according to WHO criteria and it revealed that 16.70% has mesangial proliferation, 20% had focal proliferation, 40% showed diffuse proliferation, 16.70% membranous type and 6.70% had advanced sclerosis.*

**Conclusions** *Whenever a patient, especially young female, presents with proteinuria and haematuria with RBCs cast, lupus nephritis should be suspected. If it is proved then renal biopsy should be done to classify into either mild lesion (class-11 or V) or severe lesions (class-111 or IV). The findings of renal biopsy can help in planning appropriate management of the patients.*

**KEY WORDS** *Lupus nephritis, Histopathological lesion, Clinical correlation*

## INTRODUCTION

Systemic lupus erythematosus (SLE) is a multi-system disease of unknown aetiology that primarily affects women of child bearing age. Auto-antibodies to nuclear and other antigens are the hall mark of the disease. The course of the disease is highly variable and unpredictable. Disease manifestations are protean, ranging in severity from fatigue, malaise, weight loss, arthritis, fever,

photosensitivity, rashes and serositis to potentially life threatening thrombocytopaenia, cerebritis, myocarditis, haemolytic anaemia, nephritis and pneumonitis.<sup>1</sup> Renal involvement in systemic lupus erythematosus is a common manifestation and a strong predictor of poor outcome. The prevalence of renal disease in eight large cohort studies consisting of 2649 SLE patients, varied from 31 – 65%<sup>2</sup>

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A wide variety of histologic changes may be seen on renal biopsies including mesangial, membranous, focal or diffuse proliferative and crescentic glomerulonephritis. The degree of active disease and scarring are factors that

can significantly affect the patients prognosis, therefore a renal biopsy is done to guide therapy by determining the activity and chronicity of the disease.<sup>3</sup>

More recently National Institute of Health (NIH) developed activity and chronicity indices.<sup>4</sup> High chronicity scores are associated with poor outcome and lack of response to immunosuppression. High activity indices are associated with poor outcome, but may be reversible, especially with aggressive treatment.<sup>5</sup> There has been some concern regarding the reproducibility of these indices in community setting.<sup>6</sup> The purpose of this study was to analyze the clinicopathological correlation of lupus nephritis.

## PATIENTS & METHODS

This study has been conducted in the Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi for a period of 2 years from January 2002 to December 2004. We enrolled 30 patients with lupus nephritis between the ages of 10 – 50 years who had clinical signs of renal involvement or asymptomatic proteinuria, haematuria along with other signs of SLE and renal impairment.

Various investigations like complete blood picture, renal function test such as blood urea nitrogen (BUN), serum creatinine, 24 hours urinary proteins and creatinine clearance were carried out. Other tests like anti nuclear antibody (ANA) and double standard DNA (Anti Ds DNA) were also done. Ultrasound was done for size, echo texture and renal parenchymal changes.

Ultrasound guided renal biopsy was performed in all patients and they were classified according to WHO classification depending upon histopathology of lupus nephritis. Patients were treated with steroids and other immunosuppressive therapy and course of the disease and analysis of clinicopathological features discussed at the end of the study.

## RESULTS

A total number of 30 patients of lupus nephritis were studied. Twenty-eight (93.3%) were female, with the male:female ratio of 1:14. The sex distribution among 30 patients was found statistically significant with  $p < 0.001$  (chi-square = 45.07). The mean age of all cases was  $31.50 \pm 19.68$  (mean  $\pm$  SD) and the age range was from 16-50 years. The maximum cases were found between the ages of 20-30 years. The distribution of cases among different age groups was non-significant with  $p > 0.16$  (chi-square = 5.16).

The most common renal presentation among these patients was proteinuria which was present in all the 30 cases, with nephritic syndrome in 18 (60%) patients, oliguria in 17 (56.60%), microscopic haematuria in 20 (66.60%) and hypertension in 21 (70.00%) patients with  $P < 0.001$  (chi-square = 63.36), which was statistically

significant. The various clinical features of SLE were also present; out of which mucocutaneous manifestations were present in 20 (66.00%) patients, arthritis/arthralgia in 26 (86.60%), serositis in 7 (23.30%), and anaemia in 20 (66.60%) patients.

The laboratory investigations showed that mean blood urea nitrogen was  $51.73 \pm 26.83$  mg/dl (mean  $\pm$  SD) with the range of 10-96 mg/dl. The mean serum creatinine was  $4.23 \pm 2.59$  mg/dl (mean  $\pm$  SD) with the range of 1.0-10.0 mg/dl. The Anti-Ds DNA titres were done in all 30 patients and it was significantly raised in all cases. The results of 24 hours urinary protein revealed that 12 (40.00%) patients had non-nephrotic range proteinuria (i.e.  $< 3.5$  gm/24 hours), 14 (46.70%) had nephrotic range proteinuria (i.e.  $> 3.5$  gm/24 hours), 4 (13.30%) patients had massive proteinuria (i.e.  $> 5$  gm/24 hours). Twenty four (80.00%) patients had 24 hours creatinine clearance less than 50 ml/minute. The mean value was  $37.10 \pm 28.4$  ml/minute.

Renal biopsy results, classified according to WHO criteria, revealed that 5 (16.70%) patients had mesangial proliferative (class-II) and 6 (20.00%) had focal proliferative (class-III) lesion. Diffuse proliferative (class-IV) was found in 12 (40.00%) patients, 5 (16.70%) had membranous (class-V), and 2 (6.70%) were having advanced sclerosis (class-VI). Biopsy findings were found statistically significant  $p < 0.02$  (chi-square = 11.25) (Table-I). Clinicopathological correlation of lupus nephritis is given in table II

TABLE - I LESIONS OF LUPUS NEPHRITIS AMONG 30 CASES

Biopsy Findings	Class	Frequency	Percentage
Mesangioproliferative Glomerulonephritis	II	05	16.70%
Focal Proliferative Glomerulonephritis	III	06	20.00%
Diffuse Proliferative Glomerulonephritis	IV	12	40.00%
Membranous Glomerulonephritis	V	05	16.70%
Advanced Sclerosis	VI	02	06.70%
Total		30	
P value $< 0.02$ ; Chi square = 11.25			



TABLE – II  
CLINICOPATHOLOGICAL CORRELATIONS  
OF LUPUS NEPHRITIS AMONG 30 CASES

Biopsy Findings	Frequency	Nephrotic Syndrome	Azotemia	Proteinuria
II	05	01 (20.00%)	01 (20.00%)	05 (100%)
III	06	04 (66.66%)	06 (100%)	06 (100%)
IV	12	08 (66.66%)	12 (100%)	12 (100%)
V	05	05 (100%)	02 (40.00%)	05 (100%)
VI	02	00	02 (100%)	02 (100%)
Total	30	18 (60.00%)	23 (76.66%)	30 (100%)

Note: Azotemia Serum Creatinine > 1.5 mg/dl.  
Proteinuria Urinary Protein > 0.5 g/24 hours.

## DISCUSSION

Lupus nephritis is a very common complication of SLE and it is commonly found in young females. In our study 28 patients were females and majority were in young age group. In the study conducted by Leaker et al<sup>7</sup> out of 135 patients, 120 were females. The median age of females at onset of nephritis was 25 years, thus highlighting the preponderance of lupus nephritis in young females.

Our biopsy findings revealed that majority of the patients (i.e. 40.00%) had diffuse proliferative and 20% had focal proliferative lesions. In a study by Esdaile et al<sup>8</sup>, out of 87 patients, 59 (68.00%) had diffuse proliferative lesion while mesangial lesion was found in 13 (15.00%), focal proliferative in 5 (6.00%), and membranous lesions in 9 (10.00%) patients. The diffuse and focal proliferative lesions have very bad prognosis as supported by various studies<sup>9,10</sup>.

Renal biopsy can be used for the prognosis and for the better management of the patients. An important clinical question is, "should a renal biopsy be performed in patients with lupus nephritis"? The answer probably depends on the type of information that a clinician expects from the biopsy results. For physicians or patients seeking data to confirm a short-term estimate of prognosis, renal biopsy would likely to be worth while.

Patients with class-III and IV lesions have the highest incidence of impaired renal function, nephrotic syndrome, and hypertension. This was proved by the study done by Torras and associates<sup>11</sup>. The present study also supports this hypothesis. Majority of the patients who were in

class-III and IV, had nephrotic syndrome and impaired renal function. Out of 12 patients of diffuse proliferative lesion, 8 (66.60%) patients had nephrotic syndrome and all the 12 (100%) had azotemia<sup>12</sup>.

In a study done by Chakrabarti et al<sup>11</sup>, biopsies were done in 35 cases which revealed 15 (42.80%) patients with diffuse proliferative and 8 (22.80%) with focal proliferative lesions. Clinically, hypertension was present in 19 (54.30%) patients, while nephrotic range of proteinuria was detected in 20 (57.20%). In our study nephrotic syndrome was present in 18 (60.00%) patients, hypertension and oliguria were present in 21 (70.00%) and 17 (56.60%) patients respectively.

In our study the mean 24 hours urinary protein was  $3.44 \pm 1.44$  gm/24 hours (mean  $\pm$  SD) and the mean serum creatinine was  $4.23 \pm 2.59$  (mean  $\pm$  SD). There is greater consensus for the value of laboratory tests as potential predictors than for non-laboratory clinical predictors or biopsy predictors, of outcome in lupus nephritis. An abnormal serum creatinine and to a lesser extent 24 hours urinary protein determinations or nephrotic syndrome, have been found to be of prognostic value in a convincing number of studies of lupus nephritis<sup>13</sup>. Thus from above discussion we can say that the renal biopsy and clinical findings can be used as a predictor of long term outcome.

## CONCLUSIONS

It can be recommended that whenever a patient especially young female presents with proteinuria and haematuria with RBCs or WBCs cast, lupus nephritis should be suspected. If it is proved then renal biopsy should be done to classify lupus nephritis into either mild lesion (class-III or V) or severe lesions (class-III or IV). These findings of renal biopsy can help for the appropriate management of patient with lupus nephritis.

## REFERENCES

- 1) Boumpas DT, Austin HA. SLE emerging concepts, Part -1: Renal neuro psychiatric Cardio Vascular, Pulmonary and haematologic disease. *Ann Intern Med* 1995; 122: 940 – 950.
- 2) Wallace DJ. The clinical presentation of SLE Lupus erythematosus. Edited by DJ Wallance, BH Halin, Baltimore, Williams & Williams, 1996, 627.
- 3) Cohen JJ, Harrington JT. Lupus nephritis, *Nephrology Forum Kid Int* : 538 – 558
- 4) Austin HA, Muenz LR, Joyce KM, Antonovych TA, Balou JE. Diffuse proliferative lupus nephritis: identification of specific pathologic features affecting renal outcome. *Kidney Int* 1984 25:689 – 695.
- 5) Balow JE, Austin HA, Muenz LR. Effect of treatment on the evolution of renal abnormalities in lupus nephritis. *N Eng J Med* 1984; 311:491 – 495.

- 6) Wernick RM, Smith DL, Houghton DC, Philips DS, Booth JL, Runckel DN, Johnson DS, Brown KK, Gaboury CL. Reliability of histologic scoring for lupus nephritis: a community-based evaluation. *Ann Intern Med* 1993;119:805 – 811.
- 7) Leaker B, Farley KF, Dowling J, Kincaid-Smith P. Lupus Nephritis: Clinical and pathological correlation. *Q J Med* 1987; 62: 163-179.
- 8) Esdaile JM, Federgreen W, Kashgarian M. Predictors of one year outcome in Lupus Nephritis: The importance of renal biopsy. *Kid Int* 1995; 41-50.
- 9) Austin HA, Joyce KM. Prognostic factors in Lupus Nephritis. *Am J Med*, 1983; 75: 382-391.
- 10) Torras A, Valler M, Danell A, Mirapeir E, Revert L. Lupus Nephritis: Clinicopathological manifestations. *Med Clin (Barc)*, 1980. 10; 75: 1-9.
- 11) Chakrabarti S, Ghosh AK. Clinicopathological study of lupus nephritis. *J Indian Med Assoc*, 1989; 96 : 268-271.
- 12) John M, Carey E, Federgreen K et al. The clinical and renal biopsy predictors of long term outcome in lupus nephritis: A study of 87 patients.
- 13) Wallace DJ, Podell T, Weiner J. SLE – Survival pattern, experience with 609 patients. *JAMA*, 1981; 245: 934-938.

# FACTORS ASSOCIATED WITH FAILURE OF EXCLUSIVE BREAST FEEDING

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## ABSTRACT

**Objective** *To find out the factors associated with failure of exclusive breast feeding practice up to the age of 6 months.*

**Design** *A descriptive study.*

**Place and Duration of Study** *The study was carried out at the well baby clinic of National Institute of Child Health, Karachi, from 1st July 2001 to 30th June 2002..*

**Patients & Methods** *Six hundred Infants, 1 to 6 month of age, were enrolled in the study. These babies were brought to the hospital for routine check-ups or vaccination. A questionnaire designed to obtain information about breast feeding pattern (exclusive or non-exclusive) and the reasons for not continuing exclusive breast feeding up to the age of 6 months was, filled.*

**Results** *Inadequate milk production was the commonest reason i.e. 71% as stated by mothers for not exclusively breast feeding their infants. Maternal employment was the reason in 11.2%. Other reasons were baby not gaining weight-5.2%, loose stools or constipation-3.3%, maternal systemic illness-3.6%, breast engorgement, sore nipples-2.6%, infantile colic-1.6% and 1.5% mothers did not exclusively breast feed their babies because they were twins.*

**Conclusions** *The most common reason for not exclusive breast feeding was inadequate milk production as stated by 71% of mothers, followed by maternal employment. Problems like baby not gaining weight, infantile colic, breast engorgement, sore nipple, twins etc were among the other causes for not exclusive breast feeding.*

**KEY WORDS** *Exclusive breast feeding, Breast feeding, Bottle feeding.*

## INTRODUCTION:

Exclusive breast feeding is extremely beneficial for both the infant and mother. Human milk has unique characteristics making it most suitable infant food. In addition to providing complete nutrition that sustains adequate growth and hydration at least till 6 months of age.<sup>1,2</sup> It also prevents allergic and infectious diseases by giving necessary immunological protection while baby's

own immune system is maturing.<sup>3,4</sup> It also strengthens the bonding between mother and infant, which is very important for the mental and cognitive development of the child. The prevalence and duration of exclusive breast feeding has declined in many parts of the world for a variety of social, economical and cultural reasons.<sup>5</sup> In our country, lack of knowledge regarding infant nutrition among mothers as well as health care professionals have contributed significantly toward this trend.<sup>6</sup> Rapid urbanization, easy availability of breast milk substitutes and their promotion through mass media have also caused significant negative impact on breast feeding practices.<sup>7,8</sup> There is an intense need to identify

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and review the factors associated with failure in order to lay down interventional strategies to promote exclusive breast feeding.

#### PATIENTS AND METHODS:

This descriptive study was carried out at the well baby clinic of National Institute of Child Health, from July 2001 to 30<sup>th</sup> June 2002. A total number of 600 mother infant pairs were enrolled in this study after informed verbal consent. The inclusion criteria were, infants up to 6 months of age either partially breast fed or bottle fed and infants born with normal vaginal delivery. Both primigravida and multigravida were interviewed regarding the breast feeding practices in their infants. Infants more than 6 months, delivered by caesarean section, previous history of hospitalization or with any major congenital malformation like cleft palate, Pierre Robin syndrome, congenital heart disease etc. were excluded from the study.

A standardized questionnaire was used to collect the data. Information was obtained about maternal demographic features like age, education and occupation as well as the reasons for not exclusive breast feeding.

#### RESULTS

Average age of mother was  $28 \pm 5$  years (range 17 – 40 years). There was no significant association between the maternal age and the practice of non exclusive breast feeding. 84% were housewives and 16% working women. 44% mothers were educated (at least primary education up to class 5).

Table I describes the reasons stated by mothers for non exclusive breast feeding. 71% of the mothers stated inadequate milk production, as the reason for non exclusive breast feeding. Maternal employment was an important factor associated with non exclusive breast feeding as reported by 11.2% of the mothers. 5.2% mothers started top feeding because they thought their babies were not gaining adequate weight. 3.6% mothers suffered from cough, fever, backache, generalized weakness etc and did not exclusively breast feed their infants. 2.6% mothers had problems like engorgement, retracted or sore nipple. 3.3% mothers stated that their infants either passed frequent loose stools or were constipated for which they supplemented top feedings, whereas 1.6% mothers started herbal water / tea on a regular basis for infantile colic. 1.5% mothers added supplementary feeds because they had twins.

#### DISCUSSION:

Exclusive breast feeding should be the norm from birth until the infants are five to six months old as it has numerous advantages, most important being lesser mortality, morbidity and cost. Unfortunately, in Pakistan, exclusive breast feeding rates are much lower than what it should ideally be.<sup>9</sup> Therefore, it is very important to identify the factors, which are responsible for non-

exclusive breast-feeding. In our study the major reason for failure of exclusive breast feeding was inadequate milk production noted in 71% cases. Various studies conducted in Pakistan and abroad showed similar results.<sup>10-14</sup>

This misconception is actually due to maternal anxiety and fear that she may not be able to produce enough milk. However with correct information, encouragement and emotional support, mother's confidence can be strengthened and she can breast-feed her child successfully. Improvement in the maternal diet; reduction in the time spent on household chores during pregnancy as well as after delivery have positive effect on breast feeding.<sup>11</sup> The best time to motivate and prepare a mother for exclusive breast feeding is during her antenatal visits. Factual information and advice given during antenatal period are much more effective than any paediatric pleadings after birth.<sup>11,15</sup>

Maternal employment was other important factor having significant negative impact on the practice of exclusive breast feeding. Sarwar SA and Mazhar<sup>16</sup> reported that 95% non working mothers breast-feed their infants, exclusive or non exclusive in contrast to 80% in working mothers. Similar observations were made by Khalil A & Khalil H<sup>17</sup> in Lahore. Chatman et al<sup>13</sup> in a study conducted in rural Jamaica noted that though the mothers were well informed of benefits of exclusive breast feeding, the constraint of employment forced them to start top feeding as well.

In order to promote the practice of exclusive breast feeding prolonged maternity leave should be given to the working mothers after the delivery. They should be taught to express and store their breast milk, which can be given to the infant with cup and spoon in her absence. Large institutions where many women are employed can have some area /room reserved for these working mothers to keep and breast feed their babies during long duty hours.

The other reasons for not continuing exclusive breast feeding found in our study were maternal ill health, breast problems, altered stool pattern (constipation / loose motions) and baby not gaining adequate weight. Similar findings have been reported in other studies.<sup>10,11,16</sup> All these problems can be solved by providing appropriate counseling to the mothers during pregnancy as well as after delivery. Active support by family, community and the entire health system can play a major role in establishing exclusive breast-feeding. Health care professionals and paediatricians can play a vital role in promoting exclusive breast feeding by providing proper anticipatory guidance, explaining optimal breast feeding practices and demonstrating correct techniques of breast feeding as well as skillful management of common problems.

**TABLE I: Reasons put forward for not breast feeding**

Factors	Infant age up to 6 months (n=600)	Percentage
Inadequate Milk Production	425	70.83%
Working Mothers	67	11.17%
<u>Maternal Medical Problems:</u>		
◆ Systemic Illness	22	3.67%
◆ Breast Problem	16	2.67%
<u>Medical Problem in Infant:</u>		
◆ Not – gaining Weight	31	5.17%
◆ Constipation / Loose Stools	20	3.33%
◆ Abdominal Colic	10	1.67%
Twin Baby	09	1.50%

**REFERENCE**

- Picciano MF. Nutrient composition of human milk. *Pediatr Clin North Am* 2001; 48: 53-67.
- Rogers IS, Emnett PM, Golding J. The growth and nutritional status of breast fed infants. *Early Hum Dev* 1997; 49 (suppl): 5143-55.
- Goldman AS. The immune system of human milk: Antimicrobial, anti-inflammatory and immunomodulating properties. *Pediatr Infect Dis J* 1993; 12: 664.
- Howic PW, Ogston SA. Protective effect of breast feeding against infections. *Br Med J* 1990; 300: 11-6.
- Jalil F. Breast feeding beliefs and practices. *Pakistan Pediatr J* 1998; 22: 22-3.
- Arif MA, Iqbal M. Knowledge and attitude about breast feeding among doctors training in paediatrics. *Pak Pediatr J*. 2000; 24: 91-101.
- Noble L, Hand I, Haynes D, Mc Veight T, Kim M. Factors influencing initiation of breast feeding among urban women. *Am J Perinatol* 2003; 20: 477- 83
- Giugliani ER. Breast feeding in clinical practice. *J Pediatr* 2000; 76: 238-52.
- Nagra SA, Gilani AH. Variations in infant feeding practices in Pakistan with socioeconomic stratification. *J Trop Pediatr* 1987; 33: 103-6.
- Ahmed M Awareness about breast feeding in Punjabi Village. *Pakistan J Med Res* 1992; 31: 161-3.
- Thaver IH, Hussain R. Determinants of decline in breast feeding in middle class families in Karachi, *Pakistan Pediatr J* 1994; 18: 19-25.
- Butter S, William M, Patterson J. Factors associated with non exclusive breast feeding among mothers of a cohort of Pacific infants in New Zealand *NZ Med J*. 2004; 117: 908-10.
- Chatman LM, Salihu HM, Roofe ME, Wheatle P, Henry D, Jolly PE. Influence of knowledge and attitudes on exclusive breast feeding practice among rural Jamaican mothers. *Birth*. 2004; 31: 265-71.
- Aghaji MN: Exclusive breast feeding practice and associated factors in Enugu, Nigeria *West Afr J Med* 2002; 21: 66-8.
- Akram DS, Agboatwala M, Shamshad S. Effect of Intervention on promotion of exclusive breast feeding, *J Pak Med Assoc*. 1997; 47: 46-8.
- Sarwar SA, Mazhar A, Azhar M. Attitude of mothers towards breast feeding their babies. *Pakistan Pediatr J* 1993; 17: 155-62.
- Khalil H, Khalil A, Professional mothers and breast feeding practices. *Ann KE Med Coll* 2000; 6: 60-1.

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# A STUDY OF ABRUPTIO PLACENTAE

Nagina Fatima Liquat, Tabussum Shoaib, Samia Shuja

## ABSTRACT

**Objective** *To determine the frequency of abruptio placentae and to find out associated risk factors and out come.*

**Study Design** *Cross-sectional study.*

**Place and Duration of Study** *The Department of Gynaecology & Obstetrics Unit II, Jinnah Postgraduate Medical Centre (JPMC), Karachi over one year period from July 2004 to June 2005.*

**Patients & Methods** *This study includes those patients who were brought to JPMC, Karachi with abruptio placentae after 28 weeks of pregnancy. Local causes of bleeding per vagina, placenta previa and ruptured uterus were excluded from the study both clinically and with the help of ultrasound.*

**Results** *Total number of deliveries during one year from July 2004 to June 2005 was 4497. Total number of patients with placental abruptio were 102, making an incidence of 1:44 deliveries (2.26%). Eight cases were booked while rest of the patients were nonbooked. Hypertension, preeclampsia (37.2%), anaemia 34.3% and grand multiparty were most common associated risk factors. Maternal age had no significant relation to occurrence of abruptio placentae. Most of the patients presented with bleeding per vaginum (93%) followed by onset of labour pains (80%). Maternal morbidity was high. Most common complication was anaemia 34.4% followed by post partum infection (> 14%.) Perinatal mortality was significantly high (62.5%). There was only one maternal death due to irreversible shock.*

**Conclusions** *Incidence of abruptio placenta is high (2.26%). Resultant maternal morbidity and perinatal mortality is significant. This calls for early detection, regular visits, and special surveillance. There should be timely referral to tertiary care centre.*

**KEY WORDS** *Abruptio Placentae, Risk factors, maternal morbidity, perinatal mortality.*

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## INTRODUCTION

Abruptio placentae is one of the dangerous complications of pregnancy<sup>1</sup> and is a significant cause of maternal morbidity and mortality<sup>2</sup>. Abruptio placentae complicates 1 : 75 to 225 deliveries ( 0.4-1.3%)<sup>3,4,5</sup> and the incidence is increasing both in black and white women<sup>6</sup>. It is a major contributor to obstetrical haemorrhage and a major cause of perinatal mortality in developing countries<sup>7</sup>.

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Abruptio placentae is associated with a markedly increased perinatal mortality, in literature reported to range between 19-87%<sup>4</sup>

Abruptio placentae can be defined as bleeding following premature separation of a normally sited placenta from the uterine wall prior to delivery<sup>1,7</sup>. The immediate cause of the separation is rupture of defective maternal vessels in decidua basalis a point of interface with the anchoring villi of the placental cytotrophoblast. Rarely bleeding can originate from the foetal placental vessels<sup>3</sup>.

Etiology of abruptio placentae is speculative and

perhaps multifactorial but a number of risk factors have been identified. These include advance maternal age<sup>8</sup>, multiparity<sup>9</sup>, cigarette smoking, drug abuse, sudden decompression, unusually short umbilical cord, preterm premature rupture of membranes<sup>10</sup>, chorioamnionitis<sup>11</sup>, folate deficiency chronic hypertension and preeclampsia, trauma and prior abruption<sup>3,4</sup>.

It is desirable to identify those pregnancies that run an increased risk of abruptio placentae so that maternal and perinatal morbidity and mortality can be reduced by carrying out preventive measures like antifibrinolytic agents and bed rest<sup>12</sup> which might avert the onset or halt the progress of abruptio placentae<sup>4</sup>. The aim of this study is to determine the frequency of abruptio placentae and to find out risk factors and maternal and foetal outcome.

### PATIENTS & METHODS:

Total number of 4497 deliveries were registered during one year period from July 2004 to June 2005 in the Department of Gynae & Obstetrics Unit II, Jinnah Postgraduate Medical Centre (JPMC), Karachi. This study includes those patients who were brought to JPMC with abruptio placentae after 28 weeks of pregnancy. A detailed case history including age, parity, history of present pregnancy and present illness, past obstetrical, family, personal and drug history was taken. Complete general physical and per abdominal examination was performed. Pervaginal examination was done after excluding placenta previa both clinically and with the help of ultrasound according to study protocol. Ruptured uterus and other local causes of vaginal bleeding were also excluded.

Investigations of each patient including blood complete picture, absolute values, platelet count, urea and creatinine, prothrombin time, activated partial thromboplastin time, urine detail report and serum fibrinogen levels was done. Fibrin degradation products (FDPs) were performed in selected cases. Intravenous line was maintained with wide bore cannula Foley's catheter was retained and strict intake and output chart was maintained. In case where vaginal delivery was decided artificial rupture of membranes was performed and syntocinon infusion was started to augment labour. Cesarean sections were performed under specific situation.

### RESULTS:

Out of 4497 deliveries, 102 cases (2.27%) were found with abruptio placentae having 95% confidence interval of proportion as 1.80-2.73. It was about 1 in 44 deliveries. Eight (7.8%) cases were booked for delivery while remaining 94 (92.2%) were non booked and were admitted in emergency. The age ranged between 18-40 years, and the mean age of 28.59 S.D. +/- 5.42 years. The maximum number of patients (39.2%) presented between the age of 26-30 years. 70.6% of the patients

were below the age of 30 years (table I). There were 22 (21.5%) primigravidas and 57 (55.9%) grandmultipara in this study. Gravidity ranged from 1-11 (Table I).

Most of the patients presented with multiple symptoms. The major clinical presentations were bleeding per vaginum 93 (91.1%) cases, onset of labour pain 80 (78.4%), distension of abdomen 65 (63.7%), pallor 64 (62.7%), loss of foetal movement 53 (51.9%), shock 43 (42.1%) and preterm, premature rupture membranes were 07 (6.8%) (Table II).

Hypertension preeclampsia were the most common associated conditions found in 38 (37.2%), anaemia 35 (34.3%) followed by 17 (16.7%) of preterm premature rupture of membranes, previous history of abruption, multiple pregnancy, folate deficiency, trauma & uterine anomaly (Table II).

TABLE: I		PATIENT'S DATA	
	No. of cases	(% of cases)	
Total number of deliveries	4497		
Number of Abruptio Placentae cases	102	2.27 (1.8-2.73) 95% CI	
Mean age ( years)	28.59 +/- 5.42		
<= 20 years	7	6.86	
21 - 25 years	25	24.51	
26 - 30 years	40	39.22	
31 - 35 years	25	24.51	
36 - 40 years	5	4.90	
Gravidity			
Primigravidae	22	21.57	
2 - 5	23	22.55	
Grandmultipara (>=6)	57	55.88	
Mean Gestational Age(years)	34.47 +/- 4.39		
Mean Birth Weight (kg)	2.24 +/- 0.85		

TABLE: II		CLINICAL PRESENTATION	
Sign & Symptoms	No. of cases	(% of cases)	
Bleeding pervagina	93	91.18	
Onset of labour pains	80	78.43	
Distension of abdomen	65	63.72	
Pallor	64	62.74	
Loss of foetal movement	53	51.96	
Shock	43	42.15	
Preterm premature rupture membranes	7	6.86	
Associated Risk Factors			
Hypertension & preeclampsia	38	37.25	
Preterm premature rupture of membranes	07	6.86	
Previous abruption	04	3.92	
Multiple pregnancy (Twin)	02	1.96	
Folate deficiency	01	0.98	
Trauma	01	0.98	
Uterine anomaly			

TABLE: III CLINICAL OUTCOME

Mode of Deliveries	No. of cases	(%) of cases
Vaginal Delivery	82	80.39
a. SVD	76	74.51
b. Asst. breech	03	2.94
c. Vacuum	02	1.96
d. Forceps	01	0.98
LSCS	19	18.62
Not delivered	1	0.98
<b>Maternal Morbidity</b>		
Anemia	35	34.31
Infection	15	14.71
Deranged coagulation profile	4	3.92
PPH	2	1.96
Couvelaire uterus	2	1.96
Renal failure	1	0.98
<b>Foetal outcome</b>		
Alive	47	46.08
Early Neonatal Death	8	7.84
Fresh Still Birth (FSB)	39	38.24
Macerated Still Birth (MSB)	17	16.67
Undelivered IUD	01	0.98

Every patient was transfused blood & fresh frozen plasma (FFP), before during or after delivery. The quantity of blood ranged between 1-6 pints, FFPs ranged 0-6 pints. Out of 102 cases 82 patients were delivered by vaginal route and in 19 cases C-section was performed (Table III). 60 patients had complication in the postpartum period because of these the maximum hospital stay was 9 days. The most common complication was anaemia 35 (34.5%) followed by infection (15 cases) (Table III). There was single maternal death in this study which was due to irreversible shock before the birth of the foetus depicting a mortality rate of 0.98%. Out of 104 fetuses 47 were delivered alive, out of which early neonatal death occurred in 8 babies who were premature and their weight ranged between 1 kg to 1.5 kg. Perinatal mortality was very high 62.5%.

#### DISCUSSION:

In the world literature incidence is reported to range from 0.4-1.3%<sup>4,5,12</sup>. The incidence in the present study is found to be 2.26% which is comparable with the figure (2%) reported by Saadia<sup>7</sup> from Lahore.

Abruptio placentae is recognized as one of the most serious complications of pregnancy<sup>12</sup> and is associated with a markedly high perinatal mortality in literature reported to range between 19-87%<sup>4,12</sup>. Karegard reported 20.2% perinatal mortality in 1986 followed by 9-10% reported by Rasmussen in 1996 from Sweden and Blomberg et al in 2001 from Norway<sup>13</sup>. In the present study, the follow up of babies in late neonatal period was not possible therefore only early neonatal death were included in the study. Our perinatal mortality is 62.5% (which is under estimated). The figure is very high when compared to the developed countries like Sweden<sup>5</sup> and Norway<sup>13</sup>. The probable reason for high perinatal mortality is that most of the patient (54.8%) came very

late and had intrauterine death at the time of admission and due to lack of optimum neonatal facilities. In a study from USA perinatal mortality was reported to be 17%<sup>12</sup>. In this study selective early C-section was performed by reducing diagnosis-delivery time to improve perinatal outcome.

In the present study abruptio placentae was found most common in the age group of 26-30 years (>39%). Few studies have reported a positive association of abruptio placentae with advanced maternal age<sup>1</sup> while other studies found no relation<sup>1</sup> which is comparable with the present series. In our study incidence of abruptio placentae in primigravidas and grandmultiparas was approximately 1:2.6. Similar figures of parity i.e. 1:2.5 are reported by Clark<sup>17</sup>. There are other studies which did not find any such relation<sup>1</sup>.

In the world literature most of the studies have shown a direct relationship of hypertension and preeclampsia to abruptio placentae. In the present study hypertension and preeclampsia were the most common associated risk factor found in 37.0% of cases. Similar has been reported by other series<sup>1</sup>.

Anaemia was an other common associated risk factor of abruptio placentae (34.3%) in this study. The suspicion of pre-existing anaemia in patients suffering from abruptio placentae is difficult to confirm because majority of the patients were admitted as emergencies and were nonbooked and prior haematological investigation is exceptional. The association of anaemia to abruptio has also been reported in other studies<sup>6,8</sup>.

There was a history of prior abruptio in 4 cases of this study. Karegard and Gennser reported that a history of previous abruptio placentae increases the risk of recurrence in a subsequent pregnancy 10 fold<sup>4</sup>, other studies have reported recurrence rate of 2-17.3%<sup>17,18</sup>.

In this study 7 (6.86%) cases of abruptio placentae presented with history of preterm premature rupture of membranes. Ananth CV et al reported that risk of abruptio was 3.58 fold higher among women with preterm premature rupture of membranes (2.9%) compared to women with intact membrane<sup>10</sup>(0.86%). Other studies have also reported association of abruptio placentae to preterm premature rupture of membranes<sup>11,19</sup>. In the present series cesarean section was performed in 18.6% of cases who had mild to moderate abruptio and presented at an early stage with alive; term size foetus or in cases where maternal condition was progressively deteriorating. In contrast to this, three quarter of deliveries were by cesarean section in a study by Blomberg in Sweden<sup>5</sup>.

Maternal morbidity was significant in this series, 34.3% developing postpartum anaemia, 14% developing postpartum infection, deranged coagulation profile in



3.9%, couvelaire uterus and postpartum haemorrhage (PPH) in 1.9% each and renal failure in 0.9% cases. In an other study<sup>12</sup> anaemia has been reported in 52%, postpartum infection in 30%, DIC in 13.6% cases. Sher G<sup>20</sup> observed DIC in 10-20% of his study patients with severe abruption and dead fetus. There was only one maternal death in his study depicting a maternal mortality rate of 0.98%. Hurd et al<sup>12</sup> reported no maternal death in his study patients.

#### CONCLUSION AND RECOMMENDATIONS:

From the results of this study we conclude that the incidence of abruption is high in this setup. Hypertension, preeclampsia anaemia, preterm premature rupture of membranes and prior abruption are common associated risk factor. Resultant maternal morbidity and perinatal mortality is quite significant.

This calls for measures to prevent either placental detachment or its deleterious effects on mother and foetus. Placental detachment can be prevented by early identification of operating risk factors and by modifying the reversible risk factors. This goal can be achieved by early booking & regular visits for special surveillance. The patients with abruptio placentae should be managed in tertiary care centre therefore timely referral and arrival at tertiary care unit, improvement in obstetrical care at tertiary level and advancement of neonatal care are necessary.

#### REFERENCES:

1. Khalid T, Ellahi N. Abruptio placentae; maternal and foetal out come. The professional 2001; vol 08, No.02: 296-300.
2. Kayani IS, Walkinshaw AS, Preston C. Pregnancy outcome in severe Placental abruption. BJOG July 2003; Vol. 110: 679 -683.
3. Goldstein GJ, Lockwood JC. Abruptio Placentae. Up to date 2005; vol. 13 No.2: www. uptodate.com.
4. Karegard M, Gennser G. Incidence and recurrence rate of abruption placenta in Sweden Obstet Gynaecol 1986; 67 : 523.
5. Blomberg KBN, Gennser G and Cuatthingius S. Placental abruption and perinatal death. Blackwell Science Ltd. Paediatric and Perinatal epidemiology 2001; 15: 290-7.
6. Ananth CV, Oyelese Y, YeoL, et al. Placental abruption in United State, 1979 through 2001; temporal trends and potential determinents. Am J Obstet Gynaecol 2005; 192 ( 1) : 191-8.
7. Saadia Z, Khan AZ, Nahid F. Fetal outcome varies

- with different grades of placental abruption. Annals 2003; vol. 9 No.1 : 40-42..
8. Ananth VC, Smulian CJ, Demissiek et al. Placental abruption among singleton and twin births in the United States: Risk factors profiles Am J of Epidemiology 2001; 153 (8) : 771 -778.
9. Thieba B, Lankoande J, Akotioga M et al. Abrupio Placentae; epidemiological, clinical and prognostic aspects with respect to a 177 case series. Gynaecol Obstet Ferlil 2003 May; 31 (5) : 429-33.
10. Ananth CV, Oyelese Y, Srinivas N, Yeo L, Vintzileos AM. Preterm premature rupture of membranes, intra uterine infection and oligohydramnios: Risk factors for placental abruption. Obstet Gynaecol. 2004 July; 104 (1): 71-77.
11. Khashoggi TY. Outcome of pregnancies with preterm premature rupture of membranes. Saudi Med J. 2004 Dec; 25 (12) : 1957-61
12. Hurd WW, Miodovinick M, Hertzberg V et al . Selective management of abruption placentae: A prospective study. Obstet & Gynaecology 1983; Vol 61, (4): 467-473.
13. Rasmussen S, Irgens LM, Bergsjop, Dalaker K. Perinatal mortality and case fatality after placental abruption in Norway 1967-1991. Acta Obstet Gynaecol Scand 1996; 75 : 229.
14. Paterson MEL. The aetiology and outcome of abruption placentae. Acta Obstet Gynaecol Scand 1979; 58 : 31-5.
15. Jakobovits AA, Zubek I, Abruptio placentae and fetal sex ratio. Acute Obstet Gynaecol Scand 1979;56:31-5.
16. Dafallah SE, Babikir HE. Risk factors predisposing to abruptio placentae. Maternal & Fetal outcome. Saudi Med. J. 2004 Sep; 28 (9): 1237-40.
17. Clark SL. Placentae previa and abruption placentae. In : Maternal Fetal medicine, 4<sup>th</sup> ed, Creasy PQ, Resnikk R, W B Saunders Company, Philadelphia, Pennsylvania 1999. p.620.
18. Hibbard BM, Hibbard ED. Etiological Factors in abruption placentae. Br. Med J. 1963; vol. 2: 1431-1436.
19. Vintzileoz AM, Campbell WA, Nochimson DJ, Weinbarum PJ. Preterm premature rupture of membranes: A risk factor for the development of abruptio placentae. Am. J. Obstet Gynaecol 1987; 156 : 1235.
20. Sher G. Pathogenesis and management of uterine inertia complicating abruptio placentae with consumption coagulopathy. Am J. Obstet Gynaecol 1977; 129: 164:

# OCULAR DISORDERS IN CHILDREN WITH DOWN'S SYNDROME

Seema Qayyum

## ABSTRACT

**Objective** *To find out the frequency and nature of ocular anomalies in children with Down's syndrome*

**Patients & Methods** *All the Down's syndrome patients attending the outdoor clinic of the department of Paediatrics Ophthalmology from June 2005 to December 2005 were included in the study. Their records were reviewed and related information regarding age and sex distribution, ocular anomalies and mental status were noted on performa.*

**Results** *Thirty seven patients with Down's syndrome reported during 7 month period. They were examined and evaluate for the characteristics and frequency of ocular conditions of these patients, 17(45.9%) were hypermetropes, 13(45.9%) emmetropes, and 4 (10.8%) myopes. Astigmatism of more than 3.00 diopters was present in 3 (8.1%), Strabismus was observed in 8 (27.8%) and eight patients had esotropia. Congenital nasolacrimal duct obstruction was present in 6 subjects (16,2%) and blepharitis in 12 (37.8 %). Nystagmus occurred in 5 (13.5 %). Brushfield spots were detected in 2 (5.4%). Lens opacities were diagnosed in 4 (10.8%) and all had successful cataract surgery.*

**Conclusions** *Significant correctable ocular problems are present in person with Down syndrome. It not connected they may interfere with binocular vision and the quality of life. Surgical intervention may be necessary for strabismus and cataracts.*

**KEY WORDS** *Ocular disorders, Dawn's syndrome, child*

## INTRODUCTION

Named after John Langdon Down, the first physician to identify the syndrome, Down syndrome is the most frequent genetic cause of mild to moderate mental retardation and associated medical problems which occurs in one in 800 live births, in all the races and economic groups.

To understand why Down syndrome occurs, the structure and function of the human chromosome must be understood. All human body cells contain 23 pairs of chromosomes except human reproductive cells half

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from each parent. Only the sex are chromosomes, not paired.

Three genetic variations can cause Down syndrome: Approximately 92% of the time, Down syndrome is caused by the presence of an extra chromosome 21 in all the cells of the individual. In 2-4%, Down syndrome is due to mosaic trisomy 21 the extra chromosome 21 is present in some, but not all the cells of the individual.

Approximately 3-4% of individuals with Down syndrome have normal paired chromosomes 21; but additional chromosome 21 material is translocated to the chromosome and is said to have translocation trisomy 21.

Person with Down syndrome have characteristic craniofacial development, such as flat occiput, and facial

appearance, Dysplastic ears, small nose, depressed nasal bridge, protruding tongue, high-arched palate, dental abnormalities and short and broad neck. Shortened extremities, short limbs, short and broad hands, short fifth middle phalanx, simian palmar creases, joint hyper extensibility or hyper flexibility, neuromuscular hypotonia, dry skin, premature aging, a wide range of intelligence quotients, and congenital heart defects.

Ocular findings in patients with trisomy 21 include lid anomalies, such as prominent epicanthal folds, upward slanting of the palpebral fissures, and rarely congenital ectropion. They may have lid infections, including blepharitis, blepharoconjunctivitis, chalazion, and hordeola.

A child with Down syndrome may have amblyopia, due to high refractive errors, strabismus or media opacities. Nystagmus and corneal ectasias may also be present. Nasolacrimal duct obstruction and Brushfield spots are more common in patients with lightly pigmented irides. Cataracts may be congenital or may occur later in life. Lens opacities may be sutural, zonular or complete. Glaucoma usually appears during infancy. Therefore, patients must be examined for corneal edema, megalocornea, increased intraocular pressure and optic nerve cupping. Previous studies describe an increased number of retinal vessels crossing the disk margin. Retinal detachments have been reported in patients with Down syndrome.

#### PATIENTS AND METHODS

The study was carried out in the department of pediatric ophthalmology of the Children's Hospital Lahore from June 2005-December 2005.

Visual acuity was evaluated according to the patient's intelligence and responsiveness. In the nonverbal patient, vision was evaluated in terms of quality (good, fair, or poor), location (central versus eccentric), and duration (maintained versus sporadic). In the verbal patient, visual acuity is assessed with optotypes. Patients with strabismus underwent a detailed examination to determine the cause for strabismus. Corneas were carefully evaluated for keratoconus or keratoglobus using a slit lamp. Cycloplegic retinoscopy was done. A dilated fundus examination was carried out.

#### RESULTS

The results of the initial ophthalmologic screening are shown in Table 1. A large number of children had strabismus; 8 children had esotropia and 3 exotropia.

During the initial visual acuity screening of the 37 individuals with Down syndrome, 12 did not co-operate well. These youngsters were mentally retarded, and/or displayed hyperactive or disruptive behaviours. Twenty Three had visual acuity assessments: In 5 patients vision screening revealed markedly poorer vision during the evaluation of visual acuity 71% of the children had either

CSM or 20/50 vision or better. These visual acuity results are based on vision with both eyes. 24 of them had bilateral high refractive errors. Eleven had strabismus.

TABLE 1. OSCULAR DISORDER		
Ocular problem	No. of patient (N.37)	percentage
Blepharitis	14	37.8%
Esotropia	8	21.6%
Exotropia	3	8.1%
Hypermetropia	17	45.9%
Myopia	4	10.8%
Astigmatism	3	8.1%
Emmetropia	13	35.13%
Brushfield spots	2	5.4%
Nystagmus	5	13.5%
Cataract	4	10.8%
Nasolacrimal duct block	6	16.2%

#### DISCUSSIONS

The faces of persons with Down syndrome display narrow interpupillary distance, upward and outward slanting palpebral fissures and epicanthus. These clinical features were of diagnostic importance before it became possible to base the diagnosis of Down syndrome on chromosomal analysis<sup>3</sup>.

Ocular and orbital abnormalities in persons with Down syndrome are common and have been reported with varying frequency in different surveys<sup>4</sup>.

We engaged in this study using an unselected young population of individuals with Down syndrome attending the outdoor clinic of paediatric ophthalmology of the children's Hospital. As noted in the Table, strabismus is more often observed in patients with Down syndrome than in the general population.

Most importantly, we found decrease vision in 22% of children enrolled in this study. This prevalence figure is much higher than the 8.5% reported by Hiles, Hoyme and McFarlane<sup>1</sup> (1974) and 12.5% observed by Jaeger<sup>2</sup> (1980). Decrease in vision in our study population was associated with strabismus and refractive errors. The prevalence of strabismus in our study was 27.7% which is in accordance with other reports which ranged from 23 to 44% (2-6). In the latter reports and as observed in our study, the majority 21.6% of patients had esotropia.

The results of this study suggest that children with Down syndrome may be at greater risk for visual impairment than previously reported and that they may present with decrease vision. Therefore, it is important that

these children be followed and treated appropriately to minimise that risk of developing amblyopia. Also, early treatment of strabismus and high refractive errors should reduce the level of amblyopia.

#### CONCLUSION:

Because of the increased prevalence of amblyopia, frequently observed refractive errors, and other ocular disorders in youngsters with Down syndrome it is paramount that these children undergo ophthalmologic examination early in life and be followed and treated appropriately. Normal visual acuity is important for any child. However, if the child is mentally retarded, as most individuals with Down syndrome are, an additional handicap or sensory impairment may further limit the child's overall functioning and may prevent the child from participating in significant learning processes. Visual behavior must be monitored by a pediatrician. Those who start to squint or show other abnormalities of gaze, visual behavior or attention or changes of appearances of the eyes or excessive watering in the first year of life should be referred for Ophthalmological review. All children should have formal Ophthalmological review,

including orthoptic assessment, refraction and fundus examination during the second year of life. The majority will have some deviation from normal and should be kept under close review. Those with no abnormality at first review should have further full eye examination at the age of four years. After age four vision should be tested at least every two years throughout life.

#### REFERENCES

1. Hiles, D.A., Hoyme, S.H. & McFarlane, F. (1974) Down syndrome and strabismus. *American Orthoptical Journal*, 24, 63-68.
2. Jaeger, E.A. (1980) Ocular findings in Down syndrome. *Trans American Ophthalmological Society*, 158, 808-845.
3. Wong, V. & Ho, D. (1997). Ocular abnormalities in Down syndrome: An analysis of 140 Chinese children. *Paediatric Neurology*, 16(4), 311-314.
4. Catalano, R.A. (1992). Ophthalmologic concerns. In S.M. Pueschel and J.K. Pueschel (eds), *Biomedical concerns in persons with Down syndrome*. Baltimore: Paul Brookes. pp. 59-68.

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# DELIBERATE SELF HARM: FREQUENCY AND ASSOCIATED FACTORS

Fatima kermani, Nadia.A.Ather, and Jamal Ara

## ABSTRACT

**Objective** *To determinè the frequency of deliberate self harm and its associated factors.*

**Study design:** *Descriptive study*

**Place and Duration of Study** *The study was conducted at NPCC (National Poison ControlCentre), medical unit 1, Jinnah postgraduate medical centre Karachi, from 1st sept-31st December 2004.*

**Patients & Methods** *A Total of 150 patients of deliberate self harm by means of poisoning who were admitted in NPCC, were included in the study. Data was retrieved from the files on a structured Performa. The variables of study include gender, age, marital status, monthly income and number of dependents and history of prior attempts.*

**Results** *Out of 150 patients, 86 patients (57%) were females and 64 (43%) males. mean age was 20years + 5 years. 71 patients (47%) were unmarried and 72 (48%) married. 100 patients had monthly income of 6000 or less. 128 patients (85%) had more than 3 dependents. 5% of patients had a prior history of deliberate self harm.*

**Conclusions** *Deliberate self harm is more common in females particularly of younger age group. Various psychosocial factors are involved in motivation. To prevent repeated acts of deliberate self harm or suicidal attempts in cases of Para suicide, an individualized plan should be made to counsel high risk individuals and to educate them by addressing different aspects of precipitating factors, as well as a proper treatment of psychiatric problem.*

**KEY WORDS** *Deliberate self harm, Suicide.*

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## INTRODUCTION:

Deliberate self harm (DSH) is also known as self injury (SI), self injurious behavior (SIB) and self mutilation<sup>1</sup>. DSH is different from suicide in terms of ending life, DSH is to mainly threatens others that one can end life, if her/his wishes are not fulfilled. DSH is far more common than suicide and vast majority of participants are females aged under 30 years<sup>2</sup>. While suicide is more common among men and in people who are separated

/ single or divorced<sup>3</sup>. Of particular recent interest has been the dramatic increase in the rate of para suicide or deliberate self harm in young men<sup>4</sup>. Another explanation is that females are more likely to use deliberate self harm as a cry for help or an extreme grab for attention. While suicidal males are more likely to genuinely want to end their lives<sup>5</sup>. Many predisposing factors are associated with DSH, mainly domestic, socioeconomic and accidental etc. socioeconomic are the main factors among men while domestic problems are common among females. They are not usually physically ill although psychological factors are highly significant as motivation. DSH is most common among those living in overcrowded conditions, in conflicts with their families, with disrupted childhoods

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and with a history of criminal behavior. Individual measures should be taken to prevent DSH and suicide on national level.

## PATIENTS AND METHODS

This was a descriptive study conducted at NPCC (National Poison Control Centre) ward 5, Jinnah Postgraduate Medical Centre Karachi, from 1<sup>st</sup> September-31<sup>st</sup> December 2004. 150 patients of deliberate self harm by means of poisoning who were admitted in NPCC during this time period were included in the study. Snake bite patients or any insect bite patients were excluded from the study. Data was retrieved from the files on a structured proforma. Following variables were included in the proforma: age, gender, and marital status, and monthly income, number of dependents and history of prior attempts. Data was analyzed using SPSS-10. Frequencies and percentages were computed to present all categorical variables and chi-square test was applied to compare the significance of proportions in these variables at  $p < 0.05$  level of significance.

## RESULTS:

Total of 150 patients were included in the study. Out of whom, 86 patients (57%) were females and 64 patients (43%) were males (Table 1). Male to female ratio was 1: 1.3. This data shows a high tendency of self harm in females than males in this study, however not significant ( $p=0.072$ ). Out of 86 female patients 30 were less than 20 years of age, 35 were between 21-25 years of age and 21 were in the age group of more than 25 years, 22 males were below 20 years of age, 17 were between 21-25 years and 25 males were in the age group of above 25 years. Insignificant difference of age distribution was observed between male and female patients ( $p=0.096$ ). Majority of female patients 51% were married while 53% males were unmarried and only 4.6% patients were divorced. (67%) patients had less than 6000 rupees monthly income. 33% had more than 6000 rupees monthly income with only 9% had more than 8000 rupees monthly income that revealed a high proportion of self harm in low economic group ( $p<0.001$ ). Out of 150 patients, 127 (85%) had more than 3 dependents. In 95% patients there was a history of prior DSH.

## DISCUSSION:

DSH is defined as any act by an individual with the intent of harming him / herself physically that may result in some harm. Also known as attempted suicide or parasuicide<sup>2</sup>. The average European rate of DSH and attempted suicide for persons over 15 years is 0.14% for males and 0.193% for females. For each age group the female rate exceeds that of the males with the highest rate among females in 15-24 age group while males are mostly in 12-34 years of age. Recently however, it has been found that the male: female ratio was 1:2 previously which is now diminishing<sup>6</sup>. According to our study male: female ratio is 1:1.3. In New Zealand more

females are hospitalized for deliberate self harm than males<sup>7</sup>. Some is true for our society where Para suicide is far more common in females particularly between 21-25 years as shown by our study. Epidemiological studies show a relationship between DSH and socioeconomic elements including limited educational achievement, homelessness, unemployment and economic dependence<sup>3, 4, 8, 9</sup>. Domestic problems being the major associated factors among females while socioeconomic condition play the major role among males in our society. Another important aspect of this issue is the relationship between Para suicide and suicide<sup>10</sup>. Although there are distinct demographic differences between those committing these two acts. As mentioned above DSH occurs more commonly in women of younger age group while suicidal rates are higher among males aged over 45<sup>3</sup>. The incidence of Para suicide is 10-20 times higher than that of suicide. Recently however, suicide rates have increased in young men and this rise has been accompanied by increase in the number of male Para suicidal admissions<sup>11, 12</sup>. In addition 30-40% of cases of repeated DSH or suicide there is a history of Para suicide and 3-10% of individuals repeat it with in 10 years of attempted suicide<sup>13, 14, 15, 16</sup>. This is also true for our society as shown by this study that 5% had a previous history of DSH. To prevent repeated attempts of DSH or suicide we need to identify the high risk groups, all circumstances and motivations around them. Although there is no single, readily identifiable high risk population, yet following represents small easily targeted groups. Those recently discharged from poison centre or psychiatric care, those with a history of DSH, young females with domestic problem sand young-middle aged male with socioeconomic burden<sup>17</sup>. Interpersonal conflicts seem to be a major precipitating factor or motivation in at least 75% of the patients who commit DSH<sup>8</sup>. Education and counseling of the high risk individuals is the main stay in order to prevent repeated DSH and suicides. The model of counseling is to help the patient become better able to functionally able to deal with the problems of life. this implies an individualized plan, including addressing the associated factors with the patients, treatment of psychiatric problems as well as the development of skills to solve external problems. This may also help the patient to become more aware of dysfunctional thinking and behavior that may become a motivation for further cognitive-behavioral therapy<sup>18, 19</sup>.

## REFERENCES

1. Ferreria de Castro E, Curia M, Pimenta F, Costa I. Parasicide and mental disorders. Acta psychiatr Scand. 1998; 97:25-31.
2. NHS centre for reviews and dissemination. unive rsity of York. Deliberate self harm. Effect health care. 1998; 4:1-11.
3. Charlton J, Kelly S, Dunnel K, Erans B, Jenkins R. Suicide deaths in England and Wales: trends in factors associated with suicide deaths. Poulation trends. 1993:71:34-42.

4. Hawton K. By their own young hands. *BMJ* 1992;304:1000
5. Gunnell D, Middleton N, Whitely E, Dooling D, Frankel S. Why are suicide rates rising in young but falling in the elderly? A time series analysis of trends in England and Wales 1950-1998. *Soc med* 2003; 57:595-611.
6. Suicide, women and Para suicide: a literature review. July.20,2004; 20-35
7. Hospitalization for intentional self harm. New Zealand health service. July 30, 2004; 40-45.
8. Clinical and socioeconomic characteristics of 368 patients. *Br J Psychiatry*. 1975,127:564-574.
9. Fredrick C,J.trends in mental health: self destructive behaviour among younger age group. Rochville,MD: national institute of drug abuse.1976 ed 132:782-798.
10. Le Farmer RDT. Assessing the epidemiology of suicide and parasuicide. *Br J Psychiatry* 1998;153: 16-20.
11. Beck P, Lazarus J, Scover R, Smith P,Routledge P. increasing rate of deliberate self poisoning, *BMJ* 1994;308:789.
12. Stark C, Smith H, Hall D. increase in Para suicide in scotland. *BMJ* 1994;308:1569-79
13. Hawton K, Fagg J. suicide and other causes of death, following attempted suicide. *Br J psychiatr* 1998;152:359-66.
14. Monk M. epidemiology of suicide. *Epidemiology Review* 1987,9:51-69.
15. Oven Stone I, Kreitmen N. two syndromes of suicide. *Br J psychiatr*.1974;124:336-45
16. Buglass D, Holding TA, Kennedy PF, Kreitmen N, Philip AE. Parasuicide in relation to suicide. in Kreitmen N ed. Parasuicide. london: John Whilley, 11977:158-83.
17. Suicide and par suicide prevention in public paces. In Berman AL ed. suicide prevention case consultations. New York: springer, 1990;234:544-566.
18. Lineham MM, Armstrong HE, Suarez A, Allmon D, Heard HL. Cognitive behavioural treatment of chronically parasuicidal borderline patients. *Arch Gen psychiatry* 1991;48:1060-1064.
19. Ettliger R. evaluation of suicide prevention after attempted suicide. *Acta psychiatr Scand* 1975;260:11-35.

# SURGERY IN THE FIELD HOSPITAL

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## ABSTRACT

*A descriptive study was conducted at Field hospital Lipa to assess the spectrum and pattern of surgical cases. The study included all the cases from March 2003 to March 2005. The purpose of study was to highlight the overlooked areas of training of a general surgeon in order to impart effective surgical care in remote areas where specialists of allied fields are not yet available. 10937 patients were referred to surgical out-patients department of whom 824 patients were admitted and 326 patients underwent surgery in main operation theatre. 1211 cases received treatment in minor operation theatre as out patients. Forty-nine cases were transferred to tertiary care hospital at Muzaffarabad. Many difficulties related to logistics and trained staff encountered. The study calls for the necessity of training of general surgeons in gynaecology / obstetrics, anaesthesia, radiology in addition to the specified training before being posted to field hospitals.*

**KEY WORDS** Field hospital, General surgeon, Tertiary care.

## INTRODUCTION

Working in the field has always been a challenge for a surgeon especially so, when the hospital setup has resources just enough to perform life saving procedures with a laboratory capable of basic investigations and no blood storage facilities. It really tests a surgeon to diagnose, operate and to achieve results comparable to that of a modern setup, without imaging facilities, modern antibiotics and post-operative care unit. The surgeon deals with all type of patients including that of gynaecology / obstetrics, Eye, E.N.T. Lack of communication and blockade of road-track dictates quick decision making for the interest of patients.

Remote areas like Lipa (Kashmir) which are not only far from big cities but also at times targeted by enemy shelling (Battle zone); the surgical setups in such areas are established to perform "limb and life saving surgery" as the battle injuries guide. These areas at times (winters) are cut off from the rest of the country (both road and telephonic communications) because of heavy snow and when road links are open, enemy fire hinders rapid transfer of cases from frontline to the hospital and from the hospital to that at peace location. Emergency as well as elective surgery is carried out in peace times.

## HOSPITAL SETTING

The field hospital at Lipa is providing health care to a population of 30,000 in addition to 7000 troops deployed at border. This is a fifty bedded hospital with a surgeon, a pathologist, an anesthetist, 4 operation theatre assistants, a dispenser, a radiographer, three ambulance drivers, one electricity generator operator, 25 personnel for administration. One main operation theatre equipped with two Boyle's apparatus, cardiac monitor and cardioverter, pulse oximeter, diathermy - monopolar and bipolar, fixed as well as standing rechargeable, OT lights and O2 electric autoclaves. Surgical instruments including O2 general sets, instruments for burr hole, vascular clamps and basic instruments of orthopaedic and gynaecology and obstetrics, were available. Operation theatre complex also include a minor operation theatre, sterilization room, recovery, surgical store, changing room and anaesthetist's office. The pathology laboratory had capabilities of performing blood complete examination, blood grouping and cross-match, blood for malarial parasites, hepatitis B surface antigen, urine complete analysis and pregnancy test. The laboratory had blood storage equipment which remained non-functional due to inconsistent electrical supply; but capabilities of blood transfusion and to deal with transfusion reactions were available. The field hospital at Lipa has an x-ray machine. Radiographs of limbs, chest, skull and abdomen are carried out but there is no facility for contrast studies and ultrasonography.

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The medical store supplies included all types of suture



materials (silk, catgut, vicryl, prolène), drains, catheters (less Fogarty catheter), chest tubes with under-water seal, simple tourniquets, bandages, multi-tailed bandages, Cremar wire splints, Thomas splints, plaster of Paris splintages, analgesics, antibiotics (ampicillin, cloxacillin, gentamicin, metronidazole), intravenous fluids (dextrose 5%, 10%, 25%, Ringer's lactate, haemaccel), antihelminthic agents and all varieties of anaesthetic agents.

All the casualties were handled at the hospital and the cases requiring tertiary hospital care were transferred to Combined Military Hospital, Muzaffarabad. For this purpose 2 ambulance vans equipped with emergency drugs and resuscitation equipment were present with trained drivers. This evacuation was by a crude jeep track of 25 kilometers and 90 kilometers of metal road i.e. a total of 115 kilometers and a traveling time of 3-4 hours. In winters, when road track is blocked, however helicopter could be asked for rapid evacuation of serious casualties.

### RESULTS

From March 2003 to March 2005, 40984 patients attended general out-patients department. 10937 patients were referred to surgical out-patients department. 824 patients were admitted to surgical ward with male to female ratio of 4.26:1. A total of 326 patients underwent surgery in main operation theatre. These cases were performed under general and spinal anaesthesia. Table 1 shows total number of surgical procedures performed in main operation theatre. Most of the cases were performed during the months of May to November; when the access to hospital was there, while the number of patients declined in winters when the tracks were blocked. But in winters, the obstetric cases and cases of neurosurgery were to be carried because of the inability to transfer to respective specialists.

1211 patients received treatment in minor operation theatre as out patients. 49 patients were transferred to tertiary care hospital at Muzaffarabad. Battle injuries, road traffic accidents, blunt and penetrating trauma contributed to 68 cases of debridement and removal of splinters under general anaesthesia.

SURGICAL PROCEDURES	NO.
Debridement / removal of splinter	68
Appendicectomy	38
Herniorraphy	26
Incision & Drainage	72
Laparotomy	05
Miscellaneous general surgical procedures	49
Orthopaedic ( closed reduction / amputation)	31
Urological procedures	03
Gynaecological / Obstetric procedures	17
Paediatric surgical procedures	08
Vascular surgery	03
ENT Procedures	01
Ophthalmological procedures	03
Neurosurgical procedures	02

### RECOMMENDATIONS

The nature of casualties, pattern of patients being treated at Field hospitals demands that the surgeons posted to remote areas should have a thorough training programme before hand like two months in gynaecology / obstetrics, one month each in Eye, ENT, radiology (for contrast studies and ultrasonography). The programme should be supplemented by two months training in the field of anaesthesiology, to enable them induction of general/spinal anaesthesia and to handle the associated complications, as well as to attain expertise in regional blocks and analgesia. A workshop on advanced trauma life support at a teaching hospital should be mandatory for a surgeon before being posted to remote areas.

### AUTHORS AFFILIATION

All authors worked in Field Hospital, Lipa, Kashmir during the study period.

# SEPTIC THROMBOPHLEBITIS OF THE INFERIOR EPI-GASTRIC VEIN SECONDARY TO FEMORAL VENOUS CATHETERISATION FOR PARENTERAL NUTRITION

JAA Awe, AM Soliman, RW Gourdie, GI Izuora

**ABSTRACT**

*The value of parenteral nutrition when indicated is well known, however its provision is associated with significant and sometimes life threatening complications. While the high flow in central veins may be preferable for administration, the use of peripheral intravenous nutrition has been growing in recent years. We present the case of an infant who had transfemoral long line insertion for administration of parenteral nutrition for management of the short bowel syndrome following massive bowel resection for midgut volvulus. The cannula passed into the inferior epigastric vein rather than the inferior vena cava and septic complications ensued. Prompt surgical management averted the potentially fatal onset of necrotizing fasciitis and the infant survived.*

**KEY WORDS** *Inferior epigastric vein, Septic thrombophlebitis, Intravenous cannula*

**INTRODUCTION:**

When adequate feeding through the alimentary tract is not possible, nutrients may be given by intravenous infusion. This may be in addition to ordinary oral or tube feeding (supplemental parenteral nutrition) or it may be the sole source of nutrition (total parenteral nutrition)<sup>1</sup>. Indications for total parenteral nutrition are well known<sup>2,3</sup>. Total parenteral nutrition (TPN) which is a solution containing amino acids, glucose, fat, electrolytes, trace elements and vitamins is usually infused through a central venous catheter inserted with full aseptic technique although a peripheral vein can be used for periods of up to one month.

Venous thrombosis or thrombophlebitis often occurs in superficial veins following cannulation for intravenous infusion. Thrombophlebitis of any vein can occur with total parenteral nutrition particularly in those of small caliber.<sup>4,5</sup> This case report describes complication resulting from femoral vein cannulation for nutrition purpose.

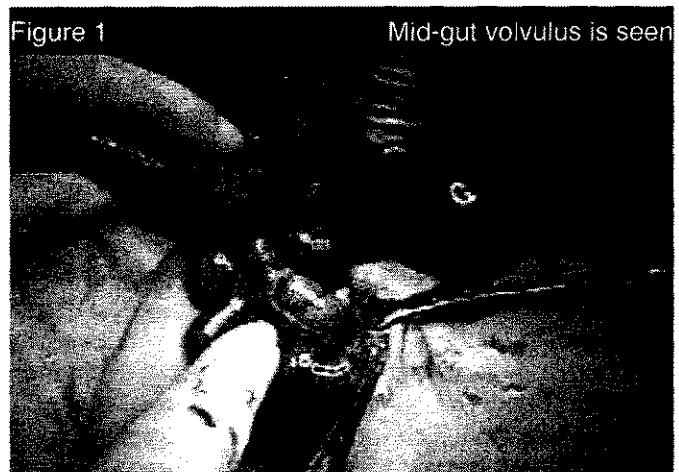
**CASE REPORT:**

A 2 year 3 month old male child with hydrocephalus was admitted through the emergency room of our hospital to the paediatric ward, having experienced fever, repeated

bouts of vomiting and relative constipation for some days. Clinical examination at that time showed a fever of 38.5°C and marked dehydration. Abdominal examination revealed the scar of a previous right inguinal herniotomy and a non-complicated left inguinal hernia. The abdomen was clearly distended but non-tender. Bowel sounds were absent and the rectum empty.

A provisional diagnosis of hydrocephalus and intestinal obstruction was made. The infant was subjected to surgery after adequate resuscitation and relevant investigations were carried out. At laparotomy, strangulated loops of small bowel extruded on opening the peritoneum.

The underlying cause of the strangulation was revealed as a mid-gut volvulus (fig 1) with its axis of rotation being



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a short mobile common mesentery. Following resection, there remained the proximal 25cm of jejunum and the colon distal to the hepatic flexure. Continuity was restored by an end to side jejuno-colic anastomosis without valve.

Postoperatively right sided femoral vein catheterization for chronic venous access and total parenteral nutrition for short bowel syndrome was carried out. He continued to make a satisfactory postoperative recovery until the 9<sup>th</sup> day when he developed high fever (40.9 C). He looked ill, vomited several times and passed loose motions. The abdomen was soft but showed localized discomfort over the right lower quadrant. Intestinal sounds were normal. The femoral venous catheter was still in situ.

Urgent abdominal ultrasound did not show any postoperative intraperitoneal collection or evidence of intestinal obstruction. Urine and blood culture were done and the femoral vein catheter was then removed and its tip sent for culture. Two hours after removal of the femoral catheter, the patient developed sudden unilateral fullness of the right lumbar region with persistent fever. Both lower limbs remained normal. A plain abdominal film showed distended bowel loops with soft tissue swelling and free gas in the right flank (fig.II).

Figure II Plain X-ray abdomen showing free gas in the right flank.



A report of abdominal ultrasound done at this stage suggested there might be an intraperitoneal collection. The differential diagnosis at this stage included septic thrombophlebitis with extravasation, postoperative deep intra abdominal sepsis and necrotizing fasciitis. The patient was subjected to re-exploration which revealed an extra peritoneal pathology. The wound was extended laterally to the right over the fullness and deepened to open the muscular and fascial planes of the anterior abdominal wall. The findings included extensive tissue oedema, inflammatory exudates and thrombophlebitis of the right inferior epigastric vein (Fig. III).

Drainage of the infected inferior epigastric vein and all

Figure III Thrombosed vein opened.



fascial planes of the right side of the anterior abdominal wall were carried out. Swabs were taken for culture and sensitivity. Two corrugated drains were placed in the superior and inferior poles of the extra peritoneal space, a suction drain in the subcutaneous tissue and the wound was closed in layers. At the same time the wound for femoral venous access was explored, deep sutures on the saphenous vein were removed, swabs were taken for culture and sensitivity and the main wound was left open.

Enterococcus Faecium was cultured from the blood, femoral vein catheter tip and necrotic material from the inferior epigastric vein as well as from the tissue exudates from the peritoneal fascial planes. This second postoperative phase was uneventful wound-wise and he was given general paediatric support with IV antibiotics, IV fluids and total parenteral nutrition for his short bowel syndrome since more than 50% of his bowel had been resected during the first surgery.

#### DISCUSSION

Paediatric indications for parenteral nutrition include surgical conditions like short gut syndrome, very low birth weight infants, mal-absorption syndrome etc. The inferior epigastric vein is formed by the union of venae commitantes accompanying the inferior epigastric artery and communicate above, with the superior epigastric vein. It joins the external iliac vein about 1cm above the inguinal ligament which in turn joins the internal iliac vein to form the common iliac vein and both join to form the inferior vena cava<sup>6</sup>. In many canterers the inferior epigastric vein is routinely cannulated to gain access for long term total parenteral nutrition because it is hidden under the clothes and does not usually interfere with movement. It is also used in a small group of patients where reliable venous access is required after venous thrombosis from

a previous catheter insertion of the commonly used veins. The inferior epigastric vein has been deliberately cannulated to gain access to the IVC on many occasions and it may remain patent for up to 18 – 20 months.<sup>7</sup>

We were able to deal promptly and manage effectively this case. Constant and meticulous monitoring should be done not only to detect complications in time but also to take immediate action in resolving them. It is usual following insertion of a venous catheter into the superior vena cava to obtain a radiograph to check position. We suggest this should be the routine when other sites are selected.

#### REFERENCES:

1. Naber AH, Rings EH, George E, Tolboom JJ, Jonkers C, Sauerwein HP. Treatment of intestinal failure by total parenteral nutrition at home in children and adults. *Ned Tijdschr Geneesk* 2005; 149: 385-90.
2. Bier ID. Peripheral intravenous nutrition therapy: outpatient office-based administration. *Altern-med-rev* 2000; 5: 347-54.
3. Bhave S, Bavdekar A. Pediatric parenteral nutrition in India. *Indian J Pediatr* 1999; 66(1 Suppl): S141-9.
4. Gharbril MS, Aranda-Michel J, Scolapio JS. Metabolic and catheter complications of parenteral nutrition. *Curr Gastroenterol Rep* 2004; 6: 327-34.
5. Nelson textbook of pediatrics: 1996; Short bowel syndrome; 286-7.
6. Raulin S, Raulin C, Greve B. Free floating thrombus in the femoral vein – a challenge in phlebologic diagnostics. *Euro J Dermatol* 2001; 11: 564-8.
7. Jackson CS, Buchman Al. The nutritional management of short bowel syndrome. *Nutr Clin Care* 2004; 7: 114-21.

# DERMATOFIBROSARCOMA PROTUBERANS IN A PATIENT WITH ALOPECIA AREATA UNIVERSALIS

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## ABSTRACT

*Dermatofibrosarcoma protuberans (DFSP) is an uncommon locally infiltrative, low grade soft tissue sarcoma. Alopecia areata universalis is a severe form of non-scarring alopecia involving the whole body. We are reporting a rare case where both of these occurred in the same patient.*

## KEY WORDS

*Dermatofibrosarcoma protuberans, Alopecia areata universalis*

## INTRODUCTION

Dermatofibrosarcoma protuberans is a soft tissue sarcoma of low grade with low metastatic potential, accounting for about five percent of all adult soft tissue tumours.<sup>1</sup> It has remained in focus because of its extremely high potential for local recurrence of up to 60 % after surgical resection, even though it is the mainstay of treatment. Wider resection margins and Mohs surgery have led to a considerable improvement in outcomes. Alopecia areata universalis refers to an unusual form of acquired hair loss involving the entire body and has been explained on the basis of an autoimmune etiology.<sup>2</sup> Various forms of medical treatment have been tried for alopecia areata universalis including minoxidil and corticosteroids. We report an extremely rare co-existence of these two unusual pathologies in a patient. Until the submission of this manuscript, the two pathologies have never been reported together.

## CASE REPORT

A 45-year-old healthy gentleman presented to a tertiary care hospital in 2002 with complaint of recurrent swellings at left shoulder region. These swellings were multiple, painless and progressively increased in size over a period of 25 years. He first noticed these swellings at the age of 20, and since then has had eight surgical resections at several district general and tertiary care hospitals. The patient reported a disease free interval of not more than two years after every surgery, following

which these swellings recurred and subsequently grew in size. Histopathology reported a diagnosis of dermatofibrosarcoma protuberans on all occasions. Patient also reported complete loss of body hair six years prior to the first appearance of these swellings, at the age of 14, clinically diagnosed to have alopecia areata universalis.

On physical examination, he was a healthy fit man with no hair on any part of the body as well as multiple large soft to firm swellings at the junction of left supra-clavicular region and left shoulder. Two of these swellings were large and measured 6 x 7 cm and 7 x 8 cm in size. With a provisional diagnosis of recurrent dermatofibrosarcoma protuberans, an excisional biopsy was carried out. Microscopic examination of the tumour revealed spindle cell lesions showing storiform pattern with mild nuclear pleomorphism and occasional mitoses. Immunohistochemically the sections were positive for CD 34 and focally positive for vimentin, but negative for smooth muscle actin, desmin and S-100. Thus the histological and immunohistochemical features clearly showed the tumour to be dermatofibrosarcoma protuberans.

A year later, the patient presented again with recurrence of swellings at the same site (Fig 1). Wide local excision of the tumour was performed with 3 cm gross margins, and tissue was sent for histopathological examination. Microscopic examination revealed a cellular spindle neoplasm with short spindle cells showing mild to moderate nuclear hyperchromasia with pleomorphism. Numerous normal and abnormal mitoses were also present. Immunohistochemistry showed the cells positive for vimentin and S-100 although CD 34 and

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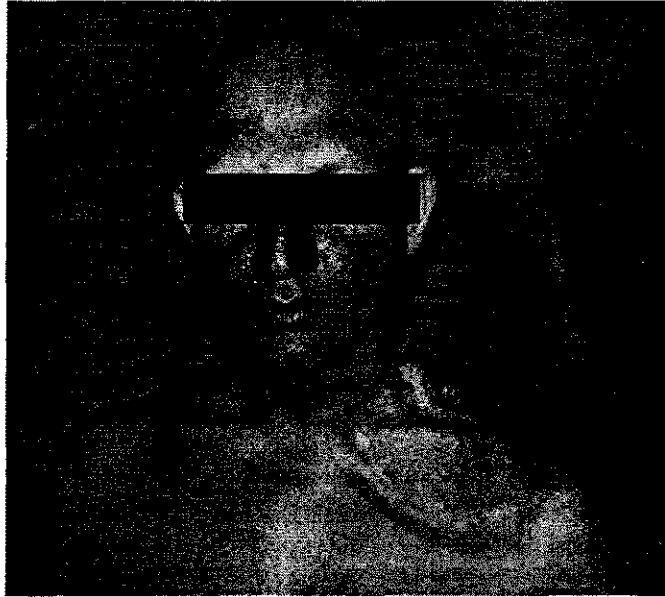
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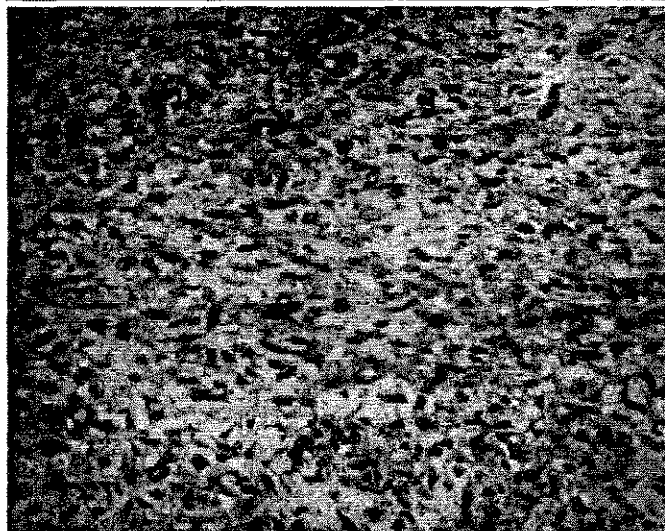
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ASMA were negative (Fig 2). The morphological and immunohistochemical results were consistent with soft tissue sarcoma with prominent neural differentiation (malignant peripheral nerve sheath tumour).

**Figure 1** Notice complete absence of scalp hair, facial hair including eyebrows, and hair on the trunk. The tumor over the left shoulder is also visible.



**Figure 2** High power magnification (Mag 40 x) showing sheets of spindly cells exhibiting nuclear pleomorphism & hyperchromasia, also note scattered mitotic figures.



## DISCUSSION

Dermatofibrosarcoma protuberans was first described in 1924 by Darier and Ferrand.<sup>3</sup> It is considered to be a fibroblastic, histiocytic, and neural tumor of low grade potential accounting for hardly five percent of all adult soft tissue neoplasm with a fairly low metastatic potential of about five percent.<sup>1</sup> The typical presentation is that of a male patient in early or middle adult life with a slow growing soft nodular cutaneous mass on the trunk, although any part of the body may be involved. Given the indolent growth and long preclinical duration, it has been proposed likely that many of these tumours appearing

in young adulthood, actually begin during childhood. Genetic analysis has shown that virtually all cases of DFSP have a translocation that involves chromosomes 17 and 22, resulting in fusion of the collagen type I  $\alpha 1$  (*COL1A1*) and platelet derived growth factor (*PDGF*) genes.<sup>4,5</sup> Surgery remains the only form of treatment, but is associated with an extremely high recurrence rate of up to 60 % with undefined or conservative excisions. However, wide excisions with a 2-5 cm margin and Mohs micrographic repair have been shown to reduce the recurrence rate to a remarkable up to 6-7 %. To date, only a handful of cases of DFSP have been reported previously from Pakistan<sup>6,7</sup>.

Alopecia literally means loss of hair and alopecia areata is the term given to a common form of non-scarring alopecia characterized by limited alopecic patches on the scalp. The more severe form of the disease includes alopecia areata totalis, which is the complete loss of scalp hair, and alopecia areata universalis, which is the complete loss of all body hair. Genetically, it is a complex trait with evidence of a role for genes of the major histocompatibility complex (MHC), the interleukin-1 cluster and chromosome 21 in the pathogenesis with the strongest association shown with HLA class II alleles<sup>8</sup>. Corticosteroids are widely used in treatment and other immune modulators such as minoxidil have also been successfully tried.

A problem with all rare diseases is that it becomes extremely difficult to establish whether their occurrence with other seemingly unrelated disorders is based on yet undiscovered common etiologic factors, or can this co-occurrence be explained on the basis of chance alone. We face a similar dilemma when reporting this co-existence of two rare pathologies, dermatofibrosarcoma protuberans and alopecia areata universalis. The two disorders to the best of our knowledge have never been previously reported to occur together. Genetically DFSP is a chromosomal rearrangement disorder, as compared to alopecia areata which is more of an aberrant autoimmune response of the body to the hair follicles, which is evident from pathological studies done on the dermal tissue of patients and controls.<sup>2,9</sup>

The final histopathological diagnosis in our case was found to be that of a malignant peripheral nerve sheath tumor (MPNST), in the background of nine previous histopathologically confirmed diagnoses of dermatofibrosarcoma protuberans made on tissue excised from the same site. One of the slides from these previous reports was available in our records and was critically reviewed and compared with the latest slides in light of the alternate diagnosis. This only confirmed the fact that the tissue excised almost two years ago showed characteristics pathognomonic of DFSP, and the tissue excised from the same site a year later represented MPNST. MPNST are malignant tumours arising from peripheral nerves or displaying differentiation along

the lines of various elements of the nerve sheath (e.g., Schwann cell, perineural cell, fibroblast). Aside from the genetic predilection in the development of these tumours, little is established about their pathogenesis. The transformation of DFSP into MPNST can not be explained on basis of the natural course of soft tissue sarcomas, although nerve sheath tumors may co-exist with angiosarcomas or skeletal muscle differentiation, an entity described as Triton tumour<sup>10</sup>.

#### REFERENCES

1. Farhood AI, Hajdu SI, Shiu MH, Strong EW. Soft tissue sarcomas of the head and neck in adults. *Am J Surg* 1990, 160:365–369.
2. Madani S, Shapiro J. Alopecia areata update. *J Am Acad Dermatol* 2000; 42: 549- 70.
3. Darier J, Ferrand M. Dermatofibromas progressifs et recidivants ou fibrosarcomes de la peau. *Ann Dermatol Syph*. 5: 545, 1924.
4. Simon MP, Pedoutour F, Sirvent N, Grosgeorge J, Minoletti F, Coindre JM, et al. Deregulation of the platelet- derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma. *Nat Genet* 1997;15:95–98.
5. O'Brien KP, Seroussi E, Dal Cin P, Sciort R, Mandahl N, Fletcher JA, Turc-Carel C, Dumanski JP. Various regions within the alpha-helical domain of the COL1A1 gene are fused to the second exon of the PDGFB gene in dermatofibrosarcomas and giant-cell fibroblastomas. *Genes Chromosomes Cancer* 1998; 23:187–193.
6. Jalali U, Rasul S, Sadiq S, Khan A, Khan A, Faisal A. Dermatofibrosarcoma protuberans. *J Coll Physician Surg Pakistan* 2005;15: 246-247.
7. Mufti T, Khan MS, Dua MU, Waqar F. Dermatofibrosarcoma Protuberans - A Rare Variant of Soft Tissue Sarcoma of Skin. An Experience of Two Cases at Ayub Teaching Hospital Complex Abbottabad. *J Ayub Med Coll* 2001;13:32-4.
8. Colombe BW, Price VH, Khoury EL, Garovoy MR, Lou CD. HLA class II antigen associations help to define two types of alopecia areata. *J Am Acad Dermatol* 1995, 3:757-764.
9. Kiuru-Kulfelt S, El-Rifai W, Fanburg-Smith J, Kere J, Miettinen M, Knuutila S. Concomitant DNA copy number amplification at 17q and 22q in dermatofibrosarcoma protuberans. *Cytogenet Cell genet*. 2001;92:192-195.
10. Heffner DK, Dnepp DR. Sinonasal fibrosarcoma, malignant schwannomas and triton tumor: a clinicopathologic study of 67 cases. *Cancer* 1992; 70:1089.