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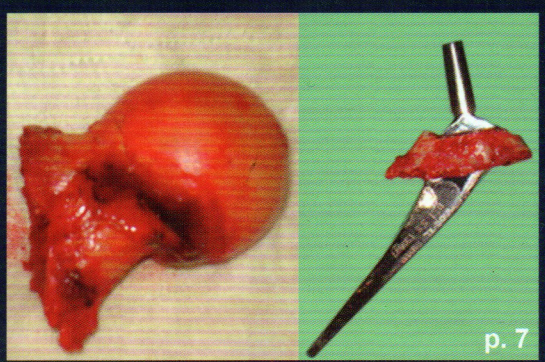
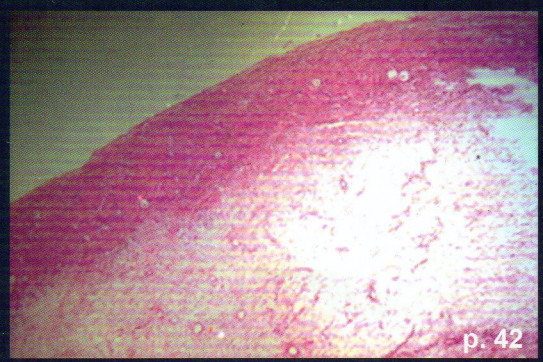
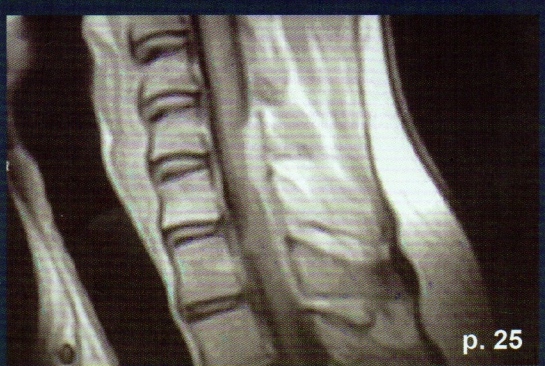


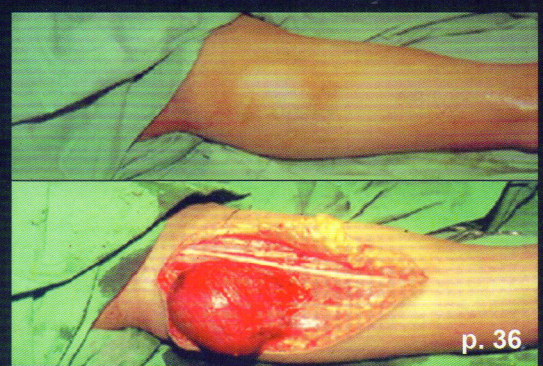
Modular prosthesis for intertrochanteric fracture



Massive oedema of ovary - Photomicrograph



Epidural lymphoma - MRI



Pseudoaneurysm

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✍ EDITORIAL

Towards a more lively Medical Journal!

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The primary purpose of any scientific journal is to communicate to those who wish or need to know, information that an author wishes or needs to impart. This can involve sharing of experience, skills and innovations and propagation of new practices. The quality of academic journals published from a country [among other parameters] is indicative of its scientific stature. The Chinese and Japanese scientists are known to take exceptional pride in publishing their research in their national journals, which ultimately grab the attention of the scientific fraternity worldwide. This is an example we Indians should emulate, and enrich further the scientific worth of the 100 odd medical journals published from our country. Mere numbers cannot ensure quality in any field, even less so in Medicine. What really matters though, is the standard of scientific accomplishments of the authors both as individuals and as members of a team.

Let us face it: many medical journals [national or international] in general could be exasperating to read, and hence, by definition, are poor transmitters of information. There are many reasons for this misery. According to the eminent UK editor, Dr Michael O'Donnell, medical writing has been infected with *'decorated scientific gothic'*. Many scientists claim that their research is very exciting and pathbreaking, but the charm is often missing in the predictable, soul-less structure and language of their academic publications.

Science ought to be fun and attractive, particularly after many months or even years of hard work; it is most unfortunate that the final offering in print can be so disappointing. Many journals do in fact insist that articles must be original, focused, brief and well motivated, and that technical terms and concepts are fully explained. Very few journals and editors, however, approve of flowery language and poetic description in a scientific journal. May be we should…… it does promote readability!

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Since the subjects of medical writing and research methodology do not form an integral part of our medical curriculum, many healthcare professionals are not well versed with its intricacies. It is indeed true that some of the contributors do not even read the instructions to authors! Editors, always cynical, consistently follow the dictum: "trust, *but always verify!*"

It is indeed a great honour, and challenge at the same time, to edit a scientific publication. A journal is as good as its editorial board, helped by the reviewers. Editorship could be quite demanding and is founded on both trust and responsibility. Editor's primary loyalty is to the journal's readers rather than to aspirant authors, the demands of the publishers or the sponsors, especially in the Indian scenario. Medical journal editors control the final gateway to publication. Hence they must protect the integrity of the scientific records by being fair and forthright and above all erudite (or knowing whom to ask!). Their task is not just accrual of information but to assist in getting their authors' messages across to readers in an effective manner, in accordance with the stated aims of the journal. Hopefully the Pushpagiri Medical Journal will be, albeit a very small, step in the right direction.

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✪ ORIGINAL RESEARCH ARTICLE

Primary modular straight stem cemented prosthetic replacement for unstable, comminuted intertrochanteric fracture in the elderly with severe osteoporosis

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Abstract

Background: The increasing number of hip fractures in the elderly, with the subset of unstable, comminuted intertrochanteric hip fractures is extremely relevant as the treatment is hampered by unsuccessful fixations and high complication rates. Osteoporosis and fracture geometry are two factors responsible for the failure of fixation in such fractures, upon which the surgeon has no control. Hence newer methods of fixation or treatment have to be opted for. **Objective:** To evaluate the functional outcome of primary modular cemented prosthetic replacement for unstable, osteoporotic intertrochanteric fractures in a selected group of patients. **Materials and methods:** A total of 34 patients with Type II and Type III unstable intertrochanteric fractures were treated with primary modular cemented bipolar prosthesis and followed up in Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla. **Results:** After surgery 94.12 % patients regained walking capacity. The functional outcome at the time of discharge was fair to excellent in 88.24% of cases. The complications were few and the major benefit was early ambulation of patients and return to pre-fracture level of activity. **Conclusion:** Primary modular bipolar straight stem cemented prosthetic replacement is probably the best option for treatment in previously independently ambulant, elderly osteoporotic patients with unstable, comminuted intertrochanteric fracture of femur.

Key words: Unstable, Comminuted, Intertrochanteric fracture, Osteoporosis, Modular cemented prosthesis

Introduction

Intertrochanteric fractures commonly occur in the elderly females. Prolonged recumbence in such cases has an adverse outcome not only in terms of patient function, but also in terms of their survival. The most important goal of treatment is an early restoration of function, which implicates an immediate, unrestricted weight bearing. Green, et al observed in 1987 that morbidity and mortality in such patients would equal those treated conservatively with traction, if the surgery performed did not permit early weight bearing[1].

While relative consensus exists about the treatment of femoral neck fractures in elderly patients, debate continues about the most appropriate treatment for unstable intertrochanteric fractures, especially in elderly patients with osteoporosis. Despite advances in internal fixation, fixing the unstable comminuted fractures in these patients still carries a high risk of failure. Elderly patients are often unable to co-operate with partial weight bearing; hence the primary stability of the device is crucial in allowing an early mobilization and preventing the cardio-pulmonary complications. Reports show that stability of the cemented prosthesis complex is significantly greater than any nail-reduction complex[2].

Early weight bearing and mobilization, and rapid return of patients to their pre-fracture status constitute the basis of primary cemented arthroplasty. While primary arthroplasty is a standard procedure for intracapsular fracture of neck of femur, little support extends to applying this procedure in the intertrochanteric fractures. Vidal, et al[3] were the first to propose primary arthroplasty in treating trochanteric fractures towards the end of 1970's. Many studies have

reported satisfactory results using unipolar/ bipolar prostheses. Stern and Angerman[4] reported their results in comminuted inter-trochanteric fractures treated by inserting Leinbach (calcar replacement) prosthesis. Primary arthroplasty is however a technically challenging procedure; all loose fragments including the greater and lesser trochanters have to be attached before cementing the stem. Also, while using a conventional unipolar/ bipolar prosthesis the head obstructs the view of the surgeon during reconstruction.

So we chose to use the modular prosthesis, where the stem is first fixed, and proper replacement of the other pieces can be done without hindrance to view by the femoral head, as occurs in case of unipolar/ bipolar prosthesis. Here only the appropriately sized neck and head are used to make up the length and off set. Also here we have the option of choosing from three different sizes of stem, three different neck lengths and different head sizes. Such a study using modular bipolar prosthesis in intertrochanteric fractures of the osteoporotic elderly patients has never been reported in the available literature.

Materials and methods

A prospective study of 34 patients was undertaken from January 2004 to July 2006 in the Department of Orthopaedics of Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla, Kerala, to evaluate the functional outcome following primary modular bipolar cemented prosthetic replacement for the unstable, comminuted, intertrochanteric fractures in elderly patients with osteoporosis.

Inclusion criteria:

1. Patients with physiological and chronological age 75 or above
2. Unstable comminuted intertrochanteric fracture: modified Evans-Jensen Type II (3 part) and Type III (4 part)
3. Patients ambulant prior to fracture

Exclusion criteria:

1. Physiological and chronological age below 75
2. Stable intertrochanteric fracture: modified Evans-Jensen Type I (2 part)
3. Patient non-ambulant prior to fracture
4. Previous ipsilateral hip surgeries
5. Osteoarthritis of hip joint

The pre-injury ambulatory status of the patients was assessed with mobility score system of Parker and Palmer[5]. All patients were assessed by plain X-ray AP view and a cross table lateral view of the involved proximal femur. Fractures were classified according to modified Evans-Jensen classification[6].

Implants

The prostheses (Fig. 1) used were modular, straight stem, bipolar, endo-prostheses (Bimod Modular Hip System INOR). They are available with stem lengths 137 mm (small), 142 mm (medium) and 147 mm (large). They are not designed to replace calcar. Bipolar XL heads were used, diameters of which range from 39 to 51 mm (with 2 mm increments); neck sizes available are short (0 mm), standard (5 mm), and long (8 mm).

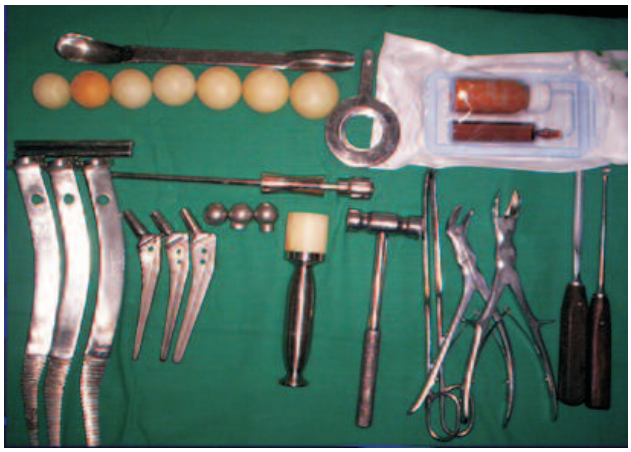

Fig. 1: Modular straight stem bipolar prostheses and accessories

Special instruments

Bimod rasp - small, medium, large
Bipolar outer head trials - ranging from 39 to 51 mm
Bimod internal head trial - short, standard & long neck
Trial stem - small, medium, large
Bimod introducer cum extractor
Internal head impactor
Head gauge

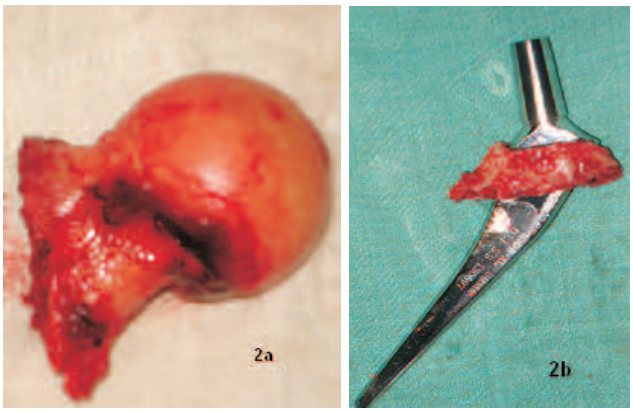

Fig. 2a Head, neck, trochanter removed;
2b Modular stem with calcar

Operative technique

- *Surgical procedure:* A straight lateral incision was put centred over the tip of the posterior border of greater trochanter, gluteus maximus and tensor fasciae latae are retracted, trochanteric bursa incised, and gluteus medius separated. The knee was flexed; hip internally rotated and extended, and short external rotators divided to visualize the posterior capsule. The fracture fragments were exposed, capsule opened in line with femoral neck, and the head, neck and trochanteric fragment removed as a single piece (Fig. 2).

- We tried to reconstruct the calcar femorale wherever possible by cutting it from the head using gigli saw. The calcar was broached and placed on the selected stem (Fig. 3) before cementing the stem to the shaft of femur.

- The femoral canal was prepared using bimod rasp, and the prosthesis stem was cemented in place using standard cementing techniques. In severe comminution, cerclage wires were used to augment fixation. Greater trochanter was stabilized with 18 gauge wires or non-absorbable prolene sutures. Trial neck and head of appropriate size was placed on the fixed stem and trial reduction performed, followed by the appropriate sized prosthesis.

  Any debris from acetabulum was removed and the joint reduced. Stability was confirmed by putting the hip through a full range of motion. Saline wash was given, capsular incision closed, trochanteric bursa and muscles sutured back, and fascia lata and skin closed in layers. Suction drain was used in all patients for 48 to 72 hours.

- *Post-operative protocol:* All the patients received prophylactic antibiotics, IV for the first five days, followed by orally until suture removal. In the immediate post-operative period the limb was kept in 30 to 40 degrees abduction.

  Active and passive movements were encouraged from the first post operative day itself; bed to chair was done on second day; patient made to stand and take a few steps using walker on third day and gait training with full weight bearing on the operated side under the supervision of an expert physiotherapy team by fourth day. Sutures were removed by tenth to twelth day, and patient discharged on being able to get out of bed and walk over level surface.

Analysis of results

- There were a total of 34 patients with unstable intertrochanteric fracture, treated with primary modular cemented bipolar prosthesis.
- The age of the patients ranged from 75 to 95 (Table 1) with a mean age of 83.4 years.

Table 1. Age distribution of patients

Age in Years	No. of patients	Percentage
75 - 80	14	41.17
81 - 85	8	23.52
86 - 90	6	17.65
91 - 95	6	17.65

- *Sex distribution:* Of the total 34 patients 05 were male (14.71 %) and 29 female (85.29 %).
- *Distribution of the side of femur:* Frequency of involvement of right and left femurs were looked for; right was involved in 22 (64.70 %) and left only in 12 (35.29 %) patients.
- *Associated Injuries:* Two patients had other injuries as well; one had a head injury with subdural hygroma, managed conservatively by our Neurosurgeon. The other had a fracture of proximal humerus (right), managed using a shoulder immobilizer.
- *Co-morbidities:* were present in 26 patients (76%), of which the most frequent (Table 2) were hypertension and diabetes mellitus.

Table 2. Co-morbid conditions present in the patients

Co-morbidities	No. of patients	Percentage
Hypertension	22	64.70
Diabetes mellitus	18	52.94
Coronary artery disease	4	11.76
Bronchial asthma	2	5.88
Hemiparesis	1	2.94

- *Types of fractures:* All the studied fractures were classified according to the modified Evans-Jensen classification. Of the total 34 patients, 22 (64.70%) had Type II [3 part] fracture with Type IIA in 14 (41.18%) and Type IIB in 8 (23.53%). Twelve patients (35.29%) had Type III [4 part] fracture.
- All patients were treated with modular bipolar cemented prostheses replacement. In six patients with Type III fracture, cerclage wire also was used to stabilize the calcar fragment.
- Bone cement was used for fixation of the femoral stem in all patients.
- The mean operative time was 96 minutes (range 82 to 124)
- The average number of units of blood transfusion was 1.9 units.
- In 32 patients (94.12%) full weight bearing ambulation could be started in 5½ days. In the

patient with fracture of humerus, and in the patient with subdural hygroma, weight bearing got delayed by one month.

- Duration of hospitalization varied from 15 to 27 days (average 18). All the patients with co-morbidities had to stay longer .

Follow up

The follow up period ranged from six weeks to 29 months, with an average of 19½ months. Regular evaluations were performed at six weeks, and three, six and twelve months, and yearly thereafter. One patient expired two months after surgery following myocardial infarction. Three patients passed away within a year of surgery due to co-morbid conditions, but were ambulant until the terminal stages. One patient got bedridden due to general debility and co-morbidities at a follow up 18 months, but she had no complaints related to the hip. Follow up of two patients was lost after two years. Ambulatory status was assessed with mobility score of Parker and Palmer, and was compared to the pre-injury status.

Roentgenographic follow up: Evaluation was done for signs of fracture healing, migration, loosening, wears, or implant failure at six weeks, three and six months (Fig. 3). It showed callus incorporating the bone fragments, even though they were not fixed to the prosthetic component. The bony envelope was responsible for the absent mobility at the site. There was no evidence of any loosening, migration, or acetabular erosion.

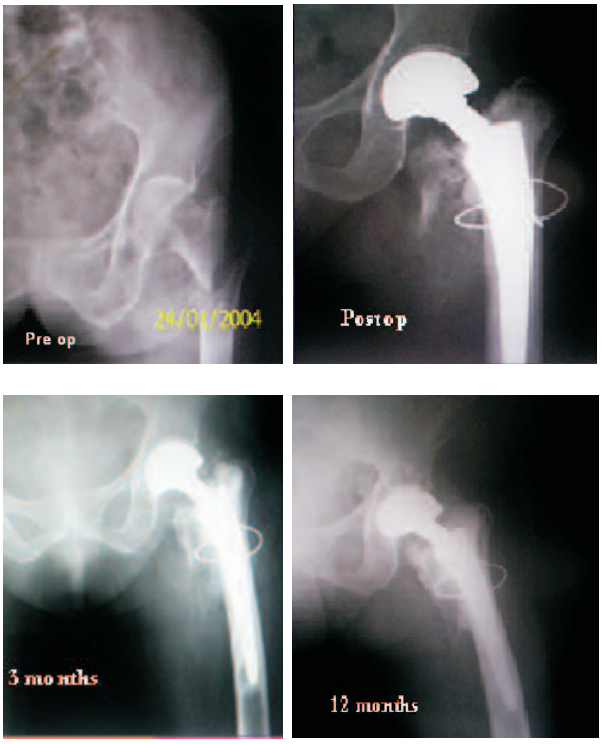

Fig. 3: Radiographic follow up of a patient

Functional outcome

The average pre-injury score was 6.8 (range 4 to 9) as assessed by Parker and Palmer scale. The average post operative mobility score at six weeks follow up was 5.4, and at sixteen weeks was 6.2 (range 4 to 9). The comparison of pre-injury and post-operative mobility score suggest that nearly all patients were able to return to their pre-injury ambulatory status without any delay. The final functional outcome (Table 3) was graded by Harris hip scoring system (HSS).

Table 3. Functional outcome of the 34 ambulant patients (HSS)

Outcome	No. of patients	Percentage
Excellent	4	11.76
Good	10	29.41
Fair	16	47.06
Poor	4	11.76

Complications

The commonest complication (Table 4) was shortening of the limb noted in six patients (18.75%). Average shortening was only 1.3 cm; as this is considered minimal, no intervention was required to be done.

Table 4. Complications following the prosthetic management

Complication	No. of patients	Percentage
Shortening	6	17.65
Respiratory infection	4	11.76
Bed sore	2	5.88
Anterior thigh pain	4	11.76

Discussion

Inter-trochanteric fractures of femur are common in elderly people with weak bone structure, and most of them are communited and unstable. The ideal implant for the treatment of unstable intertrochanteric femoral fractures is still a matter of debate. The dynamic devices popularized as sliding screw/ side plate, telescoping nail, dynamic hip screw, and sliding hip screw are currently in wide use as reliable methods of internal fixation, even though the operative technique is not always easy. The poor mechanical properties of the porotic bone in the elderly patients do not usually provide firm fixation for the screws. Surgical failure due to loosening has been documented by disengagement and intrapelvic protrusion of the sliding screws, and the cutting out of side plate screws. Various implants like trochanteric stabilization plates and Medoff plate have been tried to prevent these complications.

Few surgeons prefer prosthetic replacement to standard internal fixation supplemented with bone cement. There are advantages and disadvantages to

each option[7]. While primary arthroplasty is a standard procedure for femoral neck fractures, little evidence is available regarding its application in intertrochanteric fractures[8, 9]. They have primarily been used as a salvage procedure in cases of failure of internal fixation[10]. Calcar replacement type of prosthesis and cemented bipolar prosthesis have been reported to be useful in such fractures in the elderly. Haentjen P, et al[11] in their study of bipolar prosthesis compared with internal fixation noted that octogenarians will usually bear weight on the involved limb as much as their psychomotor abilities will allow, and the patients in the arthroplasty group were able to walk with full weight bearing without fear of losing their balance. Similar findings were noted in our study as well, and rehabilitation was easier. In another study Haentjen P, et al[12] also strongly suggest that early mobilization with full weight bearing has to be the objective of treatment. They also propose that older patients with severe osteoporosis or comminution, and non-unions could benefit better from bipolar prosthetic replacement in intertrochanteric fractures.

To the best of our knowledge, the use of modular bipolar cemented straight stem prosthesis as primary treatment in the elderly osteoporotic has not been reported in the available literature. Fixation of the modular prostheses with cement allows immediate full weight-bearing; availability of different neck lengths due to the modularity of the implant allows improved equalization of limb lengths and stability of the hip joint; long stems are useful in treating the distal disease; and the survival of these prostheses is excellent over the shortened life span of these patients[13].

Infection may occur after either arthroplasty or internal fixation, but the risk is highest in patients who require an arthroplasty after internal fixation has failed. The rate of infection in one study of femur with a pathological fracture that had been treated with arthroplasty was one to three percent[14]. In the present study with bipolar prosthesis we did not encounter any episode of deep sepsis until the last follow up.

The mean operative time in the present study was 96 minutes (range 82 to 124). This was slightly longer than the time of 69 minutes (35 to 130) reported in Chan K C, et al[8] series. The age, gender, pre-fracture health status and social dependency before fracture are also important factors determining functional recovery after hip fracture. Direct comparison of these with other studies is difficult.

In our study 94.12 % patients regained walking capacity after surgery. We had 41.17% good to excellent, 47.06 % fair, and only 11.76 % poor results as per the Harris hip score system for functional evaluation. Using mobility score of Parker and Palmer we found that nearly all patients were able to return to their pre-injury ambulatory status without delay. This proves that our surgical technique permits a more rapid recovery with immediate weight-bearing, and maintenance of a good level of function, with little risk of mechanical failure.

Roentgenographic follow up in our study showed new bone formation incorporating the bone fragments, even though they were not fixed to the prosthesis. Haentjens P, et al[12] reported similar findings. They state that new bone formation takes place in the medial and posterior aspects of femur, which bear the load in compression.

The rate of dislocation, as reported in literature[15] varies between zero and seven percent, but we did not have even a single dislocation of the modular prosthesis. Dislocations usually occur due to faulty version or length of stem. The maximum shortening in our study was only 1.3 cm, which can be considered insignificant.

➢ Advantages of modular bipolar prosthesis

1. Reconstruction of calcar and the greater trochanter fragment is easier with this technique than with ordinary bipolar or unipolar prosthesis.
2. Prosthesis length can be corrected to a certain extent using proper neck length, thus preventing limb length discrepancy.
3. Conversion to a total hip is possible, in case of acetabular erosion in follow up.
4. No unusual medical or surgical complications were encountered in this study compared with other published reports on internal fixation and endoprosthetic replacement .

➢ Limitations of the study

1. It included only a limited number of patients
2. Follow up period was relatively short. Potential long-term problems like loosening, acetabular erosion and stem failure need longer follow up
3. A control group treated with sliding hip screw was not considered
4. Cost effectiveness of the surgical intervention was not addressed

Conclusion

Primary modular straight stem cemented bipolar prosthetic replacement is a viable option for treatment in previously independently ambulant, elderly osteoporotic patients with unstable, comminuted intertrochanteric fracture. The patients' rapid return to pre-fracture level of activity significantly reduces the incidence of complications related to immobility as well. Early walking with full weight bearing is the major benefit and goal of the procedure.

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✪ ORIGINAL RESEARCH ARTICLE

Clinical profile of Congenital malformations at a Tertiary care centre

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Abstract

Background: Congenital malformations are one among the leading causes of mortality in the present era and contribute significantly to chronic morbidity. **Objectives:** To determine the incidence and clinical profile of congenital malformations at a tertiary care centre. **Design:** Cross sectional study. **Setting:** A tertiary care neonatal unit in a Medical College of Central Kerala. **Subjects:** All babies born during a period of one year. **Methods:** Detailed clinical assessment of all babies and relevant investigations in indicated cases. Congenital anomalies found out were classified system-wise. A control group of normal newborns during the same study period also was assessed and comparison was made with the study group regarding variables like gender, birth order and mode of delivery, gestational age, birth weight, birth asphyxia, maternal age, socio-economic status, maternal illnesses and antenatal problems. Chi-square test was used for statistical analysis. **Results:** The incidence of congenital anomalies was 7.3% in the study period. Of these 53.7% were major anomalies and the rest (46.3%) were minor anomalies. Out of the major anomalies, CVS (31.03%) and GIT (31.03%) showed highest incidence, whereas minor anomalies had maximal involvement of musculoskeletal system (48%). In the group of newborns with congenital anomalies there was a male predominance (72.2%), in contrast to the control group where male distribution was only 52%. Need for lower segment caesarean section was found higher in the congenital anomalies group (61.1% /control group 42.7%). Higher incidence of birth asphyxia was found in the study group (18.5% /7.3% in the control group). Low socio-economic status had a significant association with congenital anomalies (MKS III, IV 48.1% in the study group compared to 31% in the control group). No significant difference was found in variables like birth order, birth-weight distribution, gestational age pattern, maternal age, maternal illnesses and antenatal problems between the groups with and without congenital anomalies. **Conclusions:** The overall incidence of congenital malformations in the study was 7.3% which was higher compared to other Indian studies. Significantly higher incidence was seen among male babies and in those from low socio-economic status. Among major congenital anomalies, CVS and GIT anomalies predominated, whereas as a whole and among minor anomalies, musculoskeletal system was affected more. Statistically significant increase in LSCS and birth asphyxia was observed in babies with congenital anomalies.

Key words: Congenital anomalies, Newborns, Incidence

Introduction

Many congenital malformations have been described and depicted even from very ancient times. There had been innumerable false beliefs associated with the birth of a malformed child. With advancement of civilization and the progress of science, these beliefs faded off and the facts related to these events became more obvious. Congenital malformation is a physical defect present in a baby at birth, caused by prenatal genetic or non genetic events; whatever be the reason, defective morphogenesis is the basic abnormality. These defects can be single, multiple, major or minor.

A congenital malformation is considered major if it has significant effects on the physiology or social acceptability. A minor malformation has only minimal effects on clinical

function, but can have a cosmetic impact. With rapid advancement of modern medicine, there has been a decline in infectious diseases, and hence the relative increase in non-infectious diseases like congenital defects, leading to substantial neonatal mortality and life-long morbidity[1]. The incidence and pattern of congenital anomalies may vary depending on the various ethnic, geographic and socio-economic factors.

Objectives

The present study is aimed to determine the incidence and clinical profile of the congenital malformations in newborns at a tertiary health care centre of South Central Kerala.

Subjects and Methods

All inborn babies in the Centre during a one year period, from June 2006 to May 2007 (except those less than 24 weeks of gestational age and stillborn) were included in the study; the reasons for exclusion being doubtful viability and ethical problems related to autopsy. They were evaluated by a detailed history and physical examination within 24 to 72 hours of age, followed by relevant investigations. In the history, family details and prenatal problems were collected and a three generation pedigree chart was drawn in those babies having anomalies.

Physical examination was done from head to foot to pick up major and minor anomalies including the tests for developmental dysplasia of hips. Weight, length, head and chest circumference, and upper and lower segments were measured as per standard techniques. Upper segment: lower segment ratio was calculated in all babies so that growth problems could be detected. In selected cases, arm span and segmental lengths were also measured. Gestational age was calculated by the New Ballard scoring system. All systems were examined to pick up anomalies. Echocardiogram was done in all babies with major malformations and in those with doubtful cardiac murmurs and abnormalities of heart sounds. Ultrasonogram of abdomen was done in all babies with anomalies. Neurosonogram, CT scan of brain and karyotyping were done in selected cases only, because of financial constraints and parental resistance to investigate the babies with obvious congenital anomalies.

The anomalies were categorized as major and minor as per standard descriptions[2]. Babies with congenital malformations were compared to normal newborns for the variables like gender, birth order, mode of delivery, birth weight, gestational age, birth asphyxia, maternal age, socio-economic status, maternal illnesses and antenatal problems. The results were analyzed and statistical significance was detected by applying Chi square.

Results

Overall frequency and sex distribution: Out of the 740 newborns studied, 54 (7.3%) had some form of congenital malformation (Table 1). Twenty nine had major congenital anomalies, and twenty five had minor. Overall, musculoskeletal system was the commonest system involved (26%), followed by cardio vascular system (20.4%) and then gastro intestinal system (16.7%), skin (12.9%), genitourinary system (9.2%), syndromes (9.2%), [Turner-1, Down-1, Pierre Robin-2, Ellis van creveld-1], CNS (3.7%) and respiratory system (1.8%). The baby with Down syndrome was born to a 36 year old primi mother, with illegal pregnancy, never subjected to antenatal sonology or other tests. Since problems were suspected in this baby, Down syndrome could be detected early and was confirmed by karyotyping. Among the major anomalies, cardiovascular system and gastro intestinal system had maximum involvement (31.03% each).

Table 1. System-wise distribution of major & minor anomalies

Total	Major anomalies	Minor anomalies	Overall incidence
CVS	9	2	11 (20.4%)
CNS	2	0	2 (3.7%)
GIT	9	0	9 (16.6%)
Musculoskeletal	2	12	14 (26%)
Genitourinary	1	4	5 (9.2%)
Skin	0	7	7 (12.9%)
Syndrome	5	0	5 (9.2%)
Respiratory	1	0	1 (1.8%)
Total	**29**	**25**	**54**

Of the 54 newborns with congenital anomalies (Table 2), 39 were males (72.2%) and 15 were females (27.8%), whereas in the control group, male babies constituted only 52%; this was statistically significant .

Table 2. Sex distribution of Congenital anomalies

Sex	Babies with congenital anomalies	Control group without anomalies
Male	39 (72.2%)	156 (52%)
Female	15 (27.8%)	144 (48%)
Total	**54**	**300**

p = 0.009

Out of the 54 newborns with congenital anomalies, majority (Table 3) were born by LSCS (61.1%) while in the control group only 42.75% required this mode of delivery. The higher rate of LSCS in the former group could be due to various other factors influencing the formation of a child with congenital anomalies or the resultant foetal problems.

Table 3. Mode of delivery and congenital anomalies

Mode of Delivery	Babies with anomalies	Control group without anomalies
Normal vaginal delivery	19 (35.2%)	155 (51.7%)
LSCS	33 (61.1%)	128 (42.7%)
Forceps/ vacuum	2 (3.7%)	17 (5.7%)
Total	**54**	**300**

p = 0.0005

The occurrence of birth asphyxia (Table 4) was higher in babies with congenital anomalies (18.5%) than in those without congenital anomalies (7.3%) revealing a significant association between birth asphyxia and congenital anomalies.

Table 4. Birth asphyxia and congenital anomalies

Birth asphyxia	Study group with anomalies	Control group without anomalies
Present	10 (18.5%)	22 (7.3%)
Absent	44 (81.5%)	278 (92.7%)
Total	**54**	**300**

p=0.017

Socio-economic background

In the present study, 48.1% of the babies with congenital anomalies belonged to modified Kuppuswami class III and IV as against 31% of those without congenital anomalies (Table 5). A significant association was confirmed statistically between modified Kuppuswami class III and IV socio-economic status and congenital anomalies.

Table 5. Socio-economic status and congenital anomalies

Modified Kuppuswami Class	Babies with anomalies	Control group without anomalies
I, II	28 (51.9%)	207 (69%)
III, IV	26 (48.1%)	93 (31%)
Total	**54**	**300**

p=0.02

In the present study there was no statistically significant difference between the group with and without congenital anomalies with regard to birth order, birth weight distribution, the gestational age pattern, maternal age, maternal illnesses and antenatal problems.

Discussion

The incidence of congenital anomalies is two percent of all live births, but increases significantly to 16% in newborns who weigh less than 1000 gm at birth. As per annual summary of vital statistics (NCHS) 2000, congenital anomalies forming 20.7% tops the list of the ten leading causes of infant death. An incidence of 1.5% for major malformations has been reported from India[2] and 9.2 to 11.3% of perinatal deaths and 12.3 to 13.8% of neonatal deaths have been attributed to them. The higher incidence of congenital anomalies in the present study could be probably accounted for by the fact that the study setting was a tertiary care centre where relatively higher numbers of complicated and referred cases are cared for, than in a primary care centre. Various studies with the incidence of congenital anomalies are Mishra et al (1989) - 1.5%, Verma et al (1991) - 3.6%, Swain S et al (1994) - 1.2%, Bhat, Babu et al (1998) - 3.7%, Grower et al (2000) - 1.78%, Patel and Lodhia (2005) - 9.5%.

Analysis of the overall distribution of malformations in the present study showed that musculoskeletal system (26%) was the commonest system involved, followed by cardiovascular (20.3%), gastrointestinal tract (16.7%), skin (12.9%), genitourinary (9.2%), syndromes (9.2%), central nervous system (3.7%) and respiratory system (2%). The congenital malformations involving the musculoskeletal system were the most common in the studies done by Singh M, et al (1982)[3], Anand, et al (1988), Chaturvedi P, et al (1988) and Bhat and Babu (1998). Congenital malformations affecting the GIT were common in studies conducted by Ghosh, et al (1963), Mishra, et al (1975) and Terry, et al (1985).

In the present study, a statistically significant increased incidence (72.2%) was seen among male babies. Various studies have reported higher incidence of malformations in males than females. Mishra, et al (1989)[2], Swain, et al (1994), Bhat and Babu (1998)[4] are a few important studies in this regard among which only Bhat and Babu found the difference to be significant. A study by J S Anand (1988) has found a greater incidence in females, while Verma (1991) found no difference in sex distribution.

In this study, majority of the babies with congenital anomalies (61.1%) were born by LSCS, which was statistically significant. The reason could be the fact that many of these babies had foetal distress and hence LSCS were resorted to. There were also a few elective LSCS following the antenatal detection of congenital anomalies in the baby. Many congenital anomalies can lead to birth asphyxia because of various reasons. So a higher than normal incidence of birth asphyxia should be expected in such children as shown by the present study.

Another significant observation in the present study was the higher incidence of congenital

malformations in babies of mothers hailing from socio-economic class III and IV in Modified Kuppuswami Scale. Though a few studies have shown a higher incidence of malformations with increasing maternal age, the present study did not approve it, may be due to the fact that high maternal age was rare in the study group.

The higher incidence of congenital anomalies with prematurity[4,5] and low birth weight[5,6] found in various studies, was not detected in our study, probably because of the smaller sample size. Also, no significant correlation was found between maternal illnesses and identifiable malformations in newborn period. Birth order and incidence of malformation is also another area studied by others, where there are varying reports of higher incidence in primi mothers[5] as well as in multiparous women observed in different studies. In the present study no such correlation could be found out, which is statistically significant.

Conclusion and Recommendations

- Overall incidence of congenital malformations in this study was 7.3%, which is higher than expected. Hence foetal diagnostic procedures and termination of pregnancy in appropriate situation should be encouraged.
- In babies born of caesarean section and babies having birth asphyxia, vigilant search should be made for congenital malformations.
- Since increased incidence of congenital anomalies was detected in babies from low socio-economic status, improvement in living conditions should be aimed to bring down the incidence of congenital malformations.

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✪ ORIGINAL RESEARCH ARTICLE

Correlation of Clinical parameters with Oxygen saturation measurements in Acute bronchiolitis

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Abstract

Introduction: Acute bronchiolitis is a viral respiratory illness causing frequent hospitalization of young infants worldwide. Diagnostic parameters to predict the needed hospital admission and treatment modalities in these infants will be helpful for the attending clinicians. **Objective:** To correlate the clinical parameters of acute bronchiolitis with pulse oximetry. **Design:** A hospital based prospective observational study of two months duration. **Methods:** Thirty infants with acute bronchiolitis diagnosed clinically were studied by comparing the clinical signs with pulse oximeter oxygen saturation. The data was analyzed and Fishers Exact test applied for statistical significance. **Results:** The maximum affected age group was from one to three months. Ninety percent of children had danger signs at admission. Of these 73.3% required intensive care, among whom 63.3% had hypoxemia (SpO_2 < 95%) as revealed by pulse oximetry. No statistical relation was observed between clinical parameters and degree of hypoxemia. The mean hospital stay was six days. Nebulized Salbutamol, though found effective in relieving respiratory distress, did not reduce the duration of hospital stay. **Conclusions:** The degree of hypoxemia in babies with acute bronchiolitis cannot be assessed by clinical parameters alone, and can be detected more accurately by pulse oximetry.

Key words: Acute bronchiolitis, Pulse Oximetry, Clinical parameters, Nebulized Salbutamol

Introduction

Bronchiolitis is the most common cause of hospital admission among infants. It is an acute infectious disease of the lower respiratory tract which causes the obstruction of bronchioles in children younger than two years, characterized by severe respiratory distress, occasionally leading to death. A recent increase in the detection rates of bronchiolitis is judged to be due to the almost universal use of pulse oximetry screening, and hospital admission is implemented based on an oxygen saturation cut off value[1]. Attempts have been made to develop and validate models to predict the need for admission and length of hospital stay in children presenting to the emergency department with bronchiolitis. The age, dehydration, increased work of breathing and initial heart rate above the 97th percentile could predict the need for admission and a longer hospital stay[2]. However, there is a lack of consensus about the optimal diagnostic criteria in this disease. Developing guidelines for the diagnosis and monitoring of children with bronchiolitis will help clinicians to make evidence-based decisions regarding the management of such patients. Hence this study was planned.

Objectives

To correlate the clinical parameters of acute bronchiolitis with oxygen saturation measurements by pulse oximetry.

Material and Methods

This study was a prospective observational study done in a tertiary care hospital in Kerala. A child was included in the study if the following criteria were satisfied: (i) Age of the child was below two years and (ii) Agreement of clinical diagnosis of bronchiolitis by two paediatricians independently. The children with underlying chronic pulmonary, cardiac and other systemic diseases and metabolic problems were excluded from the study.

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After obtaining consent from parent/ guardian, the proforma was filled up asking the parent and by reviewing the case files of the patient. Each child was assessed clinically and the oxygen saturation measurement was done using a pulse oximeter. Chest skiagram was taken for 25 babies.

The statistical significance of the findings was tested using Fishers Exact test. The study was approved by the Ethics Committee of the Institution.

Results

The data collected from 30 children with acute bronchiolitis were analyzed.

1. Age distribution: The age of the patients ranged from 30 days to 10 months. Mean age was three and half months. 50% of children were aged below three months.

Table No. 1: Age distribution

Age (months)	No.of children	Percentage
1 - 3	15	50.0
3 - 6	13	43.3
> 6	2	6.6

2. Sex distribution: Majority of the children studied were males (63.3%).

3. Presenting complaints: All children had complaints of cough and 93.3% had respiratory distress and feeding difficulty.

Table no. 2: Presenting complaints of study children

Presenting complaints	No. of children	Percentage
Cough	30	100.0
Respiratory distress	28	93.3
Feeding difficulty	28	93.3
Coryza	15	50.0

4. Family contact with respiratory infection: There were 20 children (66.6%) who had a history of contact with respiratory infections from family members.

5. Duration of ICU stay: Of the 22 children who required ICU admission, 72.7% needed ICU stay from two to seven days.

Table No. 3: Duration of ICU stay

ICU stay	No. of children	Percentage
< 2 days	5	22.7
2 - 7 days	16	72.7
> 7 days	1	4.54

6. Duration of hospital stay: The mean hospital stay was six days. The distribution of the duration of hospital stay is given in Table no. 4.

Table No. 4: Duration of hospital stay

Hospital stay	No. of children	Percentage
< 4 days	6	20.0
4 days - 1 week	14	46.6
> 1 week	10	33.3

7. Findings from clinical examination

Of the 30 study children 90% presented with one or more danger signs (feeding difficulty, cyanosis etc.) at the time of admission. Of these 63% had hypoxemia (SpO_2 < 95%). This result is shown in Table no. 5.

Table No. 5: Danger signs and SpO_2

Danger signs	SpO_2 < 95%	%	SpO_2 > 95%	%	Total %
Yes	17	63.0	10	37.0	27 (90.0)
No	2	66.7	1	33.3	3 (10.0)
Total	19	63.3	11	36.7	30

p = 0.70

Of the 26 children with respiratory rate below seventy, 57.7% has oxygen saturation less than 95%. No significant association was found between the respiratory rate and oxygen status.

Table No. 6: Respiratory rate and SpO_2

Respiratory rate	SpO_2 < 95%	%	SpO_2 > 95%	%	Total (%)
< 70	15	57.7	11	42.3	26 (86.6)
70 - 80	2	100.0	-	-	2 (6.7)
> 80	2	100.0	-	-	2 (6.7)
Total	19	63.3	11	36.7	30

p = 0.58

There were 21 children from the study group who were observed to have varying grades of chest retraction, especially subcostal retraction. The findings are presented in Table no. 7.

Table No. 7: Degree of chest retraction and SpO_2

Chest retraction	SpO_2 < 95%	%	SpO_2 > 95%	%	Total (%)
Mild	13	76.5	4	23.5	17 (80.9)
Moderate	2	66.7	1	33.3	3 (14.3)
Severe	1	100.0	0	0	1 (4.8)
Total	16	76.2	5	23.8	21

p = 0.69

In the study group 25 children had chest skiagram and 52% had severe bronchiolitis. The relation of skiagram findings and oxygen saturation is given in Table no. 8. Majority of those with hypoxemia had severe (grade 3) bronchiolitis .

Table no. 8. Skiagram findings and SpO_2

Skiagram findings	SpO2 <95%	%	SpO2 >95%	%	Total %
Grade 1 (hyperinflation)	5	29.4	5	25.0	7 (28.0)
Grade 2 (1+streaky shadows)	4	23.5	1	12.5	5 (20.0)
Grade 2 (1+pneumonia)	8	47.1	5	62.5	13 (52.0)
Total	17	68.0	8	32.0	25

p = 0.73

The treatment given to these children are presented in Table no. 9. Nebulized Salbutamol was given to all children in addition to conventional methods.

Table No. 9: Treatment given

Treatment	No of Children	Percentage
Humidiated oxygen	28	93.3
Antibiotics	30	100.0
Salbutamol	30	100.0
Corticosteroids	10	33.3

The children were discharged once complete recovery was achieved. Follow up was done after one week. None of the children in the study group were found to be symptomatic. No mortality was reported.

Discussion

Acute bronchiolitis is a viral infection of lower respiratory tract[3]. The results obtained from the study clearly indicate that the maximum age group affected was below six months. Bronchiolitis most commonly presents in infants aged three to six months[4]. In this study majority of the children were aged from one to three months.

Diagnosis of bronchiolitis is clinically based on history and findings from physical examination[5]. Cough and respiratory distress were the main presenting complaints. Half of them were reported to have coryza. These complaints have high diagnostic value. Bronchiolitis typically has a coryzal phase for two to three days, which precedes the onset of other symptoms[3].

It is seen that children who had contacts with respiratory infection from family members have higher incidence of bronchiolitis. Along with the clinical assessment, pulse oximetry was performed to assess the degree of hypoxemia in acute bronchiolitis. Lower oxygen saturation levels on hospital admission predict more severe disease and longer length of stay[6,7]. At the time of admission 63.3% babies had hypoxemia.

Most of the babies (90%) presented with danger signs like feeding difficulty, cyanosis etc. Majority of the babies (63.0%) presenting with danger signs had low oxygen saturation (less than 95%), though no statistically significant relation could be found out. More cases have to be analyzed for a definite correlation.

Of the study children 76% had either fine crackles or expiratory wheeze. Fine inspiratory crackles in all lung fields are a common finding in acute bronchiolitis[4,8].

Majority had mild chest retractions especially subcostal retraction. Dyspnoea with subcostal, intercostal and supraclavicular recession were commonly seen in infants with acute bronchiolititis[5,8,9,10]. Degree of chest retraction and oxygen saturation values were assessed and were found to be statistically not significant.

Regarding the skiagram findings, the typical early radiological changes seen in viral bronchiolitis is hyperinflation. If superadded bacterial infections occur, changes pertaining to pneumonia may be seen. Hence chest skiagram should be considered in those infants where there is diagnostic uncertainty or an atypical disease course. This study revealed that 52% babies had secondary bacterial infection.

In the treatment oxygen was administered to nearly all children in the study group. Careful assessment of respiratory status and oxygenation form the most critical aspect of caring for children with viral bronchiolitis. Antibiotics are administered for secondary bacterial infection as evidenced by the skiagram findings. Salbutamol was administered to all cases in the study group. A modest clinical improvement is observed when a trial of nebulized β_2 agonist was given with oxygen for babies with acute bronchiolitis[11]. Steroids were administered to few children, but its efficacy is doubtful.

The children on discharge from the hospital were active, alert and afebrile. Follow up after one week revealed the children to be healthy and asymptomatic.

Conclusions

Bronchiolitis is a disease with early age of onset, less than three months, in our set up. A diagnosis of acute bronchiolitis should be considered in an infant with nasal discharge, a wheezy cough and in the presence of fine inspiratory crackles/ high pitched

expiratory wheeze. Respiratory distress may be the presenting feature often associated with feeding difficulty. Infants with oxygen saturation below 95% who have severe respiratory distress or cyanosis should receive supplemental oxygen.

Pulse oximetry should be performed in every infant who comes to the hospital with acute bronchiolitis.

Severity of the disease can be assessed by clinical features i.e., poor feeding (< 50% of usual fluid intake in preceding 24 hrs), respiratory rate > 70/minute, respiratory distress and severe chest wall recession. These parameters can be used as a clinical scoring system.

Adequate and timely intervention can give good results in almost all patients. Complete recovery within minimal duration of hospital stay can be achieved.

Further research can be done on measures to prevent bronchiolitis so that improvement can be made in health care system. Also studies are yet to be done in the field of developing effective immunization against bronchiolitis, affordable to the common people.

Acknowledgement

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✪ ORIGINAL ARTICLE

First dental visit of a child: A retrospective study

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Abstract

Aims and Objectives: To know the average age at which parents first seek dental care for their children and to find the common reasons for seeking dental care in their first visit to the Department of Pedodontics and Preventive Dentistry, Pushpagiri College of Dental Sciences, Tiruvalla, Kerala. **Materials and Methods:** About 1200 patient records from the Department of Pedodontics and Preventive Dentistry were scrutinized, of which 500 were considered for the study. From the selected records, age and reason for the first dental visit was noted in a data sheet. Patients were categorized into three groups based on their age; the reasons for their visit were divided into ten categories, and the percentages calculated. **Results and Conclusions:** The average age of the first dental visit of children is seven years of age, dental caries being the commonest indication. It is also concluded that the awareness level regarding the importance of the first dental visit was very low in the study population.

Key words: First dental visit of child, retrospective study, first year of life, dental caries, prevention and orientation.

Introduction

The first dental visit is an important milestone in the child's life, and a timely visit should be an essential part of the child's general health care[1]. Traditionally, the recommended time for the first dental visit has been at three years of age. The rationale for choosing this later age was that children were more manageable, and treatment was more efficient. By three years of age, however, poor oral hygiene or improper feeding habits might already have compromised oral health[2].

The American Association of Paediatric Dentistry (AAPD) recommends that the first oral examination should occur within six months of the eruption of the first primary tooth, but not later than 12 months of age[2]. Conversely, the American Academy of Paediatrics currently recommends that children should be referred for an initial dental evaluation at 24 months of age[3]. The purpose of this dental visit is to *'lay the foundation on which a life time of preventive education and dental care can be built, in order to help assure optimal oral health into childhood'.*

Year one dental visit helps to give an anticipatory guidance and the establishment of a dental home. **Dental home** is a comprehensive, continuous program which provides preventive oral health supervision and emergency care. An early dental intervention provides an opportunity to supplement the oral health education for parents in areas such as proper oral hygiene and prevention of early childhood caries. Such intervention may also allow children to become comfortable in the dental departments[4].

This study was conducted in order to determine the average age at which the parents first seek dental care for their children, and also to ascertain the common reasons for seeking dental care at the first dental visit in Tiruvalla, Kerala, India.

Materials and methods

The patient records from the Department of Pedodontics and Preventive Dentistry, of The Pushpagiri College of Dental Sciences, Tiruvalla were utilized for this retrospective study.

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A total 1200 patient records were scrutinized, of which 500 were considered for the study. Records that did not show the age of the patient or had inadequate details regarding the cause for the first dental visit were discarded. The sampling method undertaken was random sampling technique. From the 500 records, the age and reason for the first dental visit was noted, and were then divided into three groups based on their age, as follows:

Group 1 : 0 - 3 yrs
Group 2 : 3 - 6 yrs
Group 3 : 6 -12 yrs

The percentage of children belonging to each group was statistically analyzed. The reasons for their visit were divided into ten categories as follows:

Group 1 : dental check up
Group 2 : dental caries
Group 3 : deposits/ bad breath
Group 4 : trauma
Group 5 : pain/ sensitivity
Group 6 : malocclusion
Group 7 : missing/ extra tooth
Group 8 : orientation
Group 9 : habits
Group10 : other infrequent reasons like cleft palate, cleft lip, mobile teeth and soft tissue lesions

Results

The average age at which parents first seek dental care for their children was found to be 7.1 ± 2.7 with a standard deviation of 2.7.

The percentage of children in different age groups reporting for their first dental visit is shown in Fig. 1. The most frequent age group was 6 to 12 years (70.7%), followed by 3 to 6 years (23%). It was lowest (6.2%) in the age group below three years.

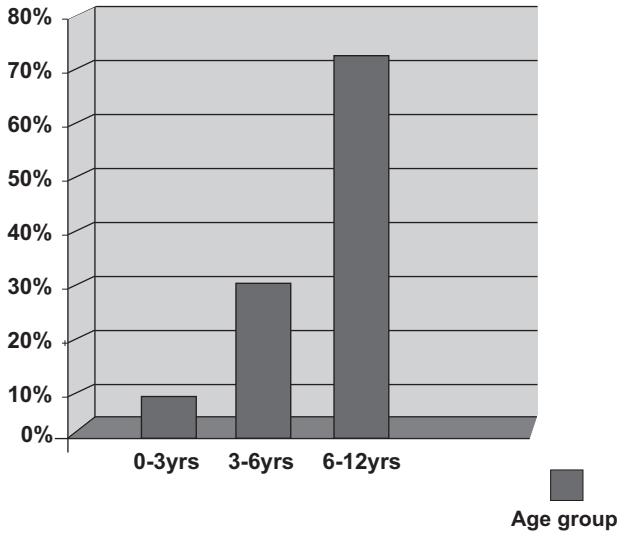

Fig 1: Frequency of first dental visit in different age groups

The different reasons for the first dental visits of the children are depicted in Fig. 2. The most common reason was dental caries (42.3%), followed by other reasons (19.2%) like cleft palate, mobile teeth, etc. Pain/ sensitivity (13.2%), malocclusion (13.2%), as a part of routine checkup (6%), trauma (2.8%), deposits/ bad breath (2.4%), habits (0.7%), missing or extra tooth and orientation (0.2%) were also observed as reasons for consultation.

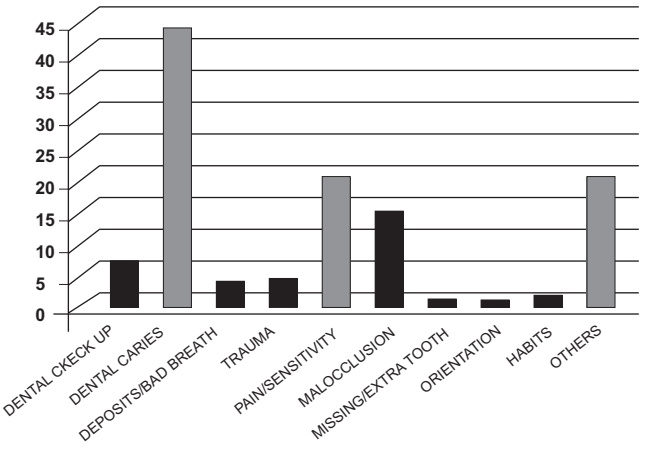

Fig 2. Reason for first dental visit

When male to female ratio was considered, the male population showed a higher frequency (53.9%) of dental visits as compared to the female population (46.1%) in all three age groups, as shown in Fig. 3.

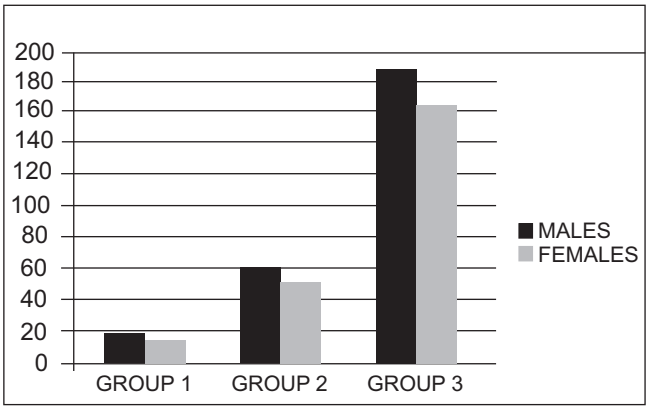

Fig 3: Male - Female distribution in different age groups

Discussion

An early dental visit is important in the light of rendering prevention-oriented intervention for the paediatric patients, and parental counseling regarding common dental diseases and the dental habits of their children. The preventive goals during an early dental visit includes improvement of oral hygiene and eating habits, informing parents about the risks posed by non-nutritive sucking, educating parents regarding traumatic injuries, how to seek emergency dental care, etc[1].

The present study revealed a very late visit of the child to the dentist and for a condition that was not mild or in a preventable stage.

Traditionally, the family physicians and paediatricians have been providing information on preventive oral health in infants, because of the early age at which these children are brought to their offices, and the fact that parents generaly accept their recommendations[5]. Awareness should also be made among these medical professionals, since they get acquainted with the children at an earlier age, as compared to the dentist.

The ideal time for the first dental visit of a child as recommended by AAPD is the first year of life. The present study shows that we are nowhere near the ideal age. Where the most common reason for the visit should have been prevention, orientation or for routine dental check up, the present study shows the reason for visit as dental caries, which is a later stage of the disease process. A similar study conducted by Meera et al[1] in Chennai also showed similar results.

There is a lack of availability of data regarding the timing of the first dental visit and the reasons for the same, in the infants and children of Indian population. Hence further studies are warranted to determine the dental awareness of parents and medical professionals in this score.

Conclusion

The results drawn from the study reveal that the most common age group of the children for their first dental visit in Tiruvalla, Kerala is six to twelve years, and the commonest reason for the consultation was dental caries.

Acknowledgement

The author wishes to thank to Dr Oommen Aju Jacob, MDS, FDS, RCS (Eng), DNB, FFDRCS (Ire) Principal, Pushpagiri College of Dental Sciences for his encouragement for the study and Mrs. Nisha Kurian, Assistant professor of Biostatistics, Pushpagiri Institute of Medical Sciences for her help in the statistical analysis.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE SERIES ARTICLE

Unusual presentations of Non Hodgkin lymphoma

Part II: An unusual case of Spinal cord (epidural) lymphoma in cervical region - T cell type

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Abstract

Non Hodgkin lymphoma (NHL) is well known for its unusual clinical presentations, varying sites of origin and spread in an unpredictable fashion. Each case of extra nodal lymphoma will have some unique feature. We worked up a series of very unusual cases of NHL, with rare clinical presentations, histopathological features, management modalities and prognosis.

This second part of the series article is discussing the case of a young male patient who presented with cervical myelopathy, which on detailed investigations and neuroimaging, turned out to be due to epidural NHL. The epidural lesion was probably secondary, as the patient had evidence of skin involvement also, in the form of multiple nodules. Histopathologically the skin lesions turned out to be cutaneous non Hodgkin lymphoma, T cell type (CD3 positive). In this patient with NHL, the spinal cord compression was produced by epidural involvement, the tumour was located in the cervical region and the cells of origin were T-cells. All these features, together with the initial clinical presentation with neurological symptoms, make it a very unusual case report.

Key words: Non Hodgkin lymphoma, T cell type, Cervical, Epidural, Spinal cord compression, MRI

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Case report

A 25 year old male patient, architect by profession, presented with pain in the right upper limb and low grade fever of one and half month duration. The pain started in the right middle finger initially, and later spread to involve the right index and ring fingers, and subsequently to the upper arm and shoulder. The pain was so severe that he had to use his left hand to operate the computer. During this period he also had intermittent low grade fever. Just prior to seeking medical attention he had noticed skin nodules over the chin and fore head.

On examination he was a thin well nourished person, with mild weakness and wasting of his right upper arm. Neck movements produced pain along the right arm. Also there was sensory impairment along C5, C6 and C7 dermatomes on the right side. There were no features of Horner's syndrome or pyramidal signs.

Considering the onset of symptoms along the distribution of C6 and gradually spreading to C5 and C7 nerve roots, the possibility of an extramedullary intradural spinal cord lesion was considered, and he was investigated on those lines.

Investigations

Most of the haematological and biochemical investigations revealed normal values. The only abnormalities observed were a mild neutrophilia, high ESR (100 mm in the first hour) and hyperkalemia (serum potassium 5.0 mmol/ L).

Serum total protein value was 7.1 gm/dl (albumin 3.6 gm/dl and globulin 3.5 gm/dl).

Peripheral smear showed a relative neutrophilia.

MRI cervical spine

T1W sagittal showed a hyperintense dorsal epidural lesion

(marked by black arrows) compressing the spinal cord (Fig. 1).

The axial view in MRI showed an ill-defined hyper-intense lesion in the paravertebral region on the right side, with extension into the spinal canal (Fig. 2), shown by arrows.

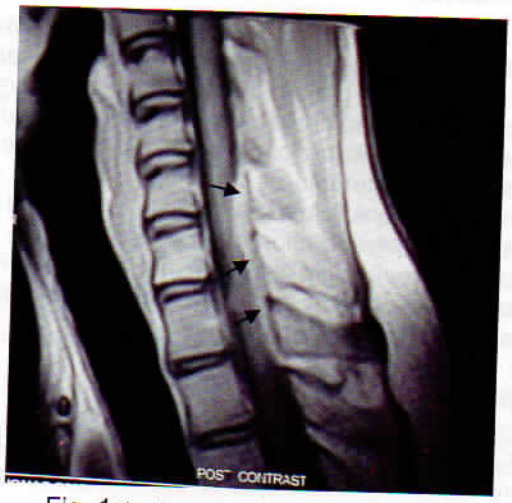

Fig. 1: Lesion extending into spinal canal

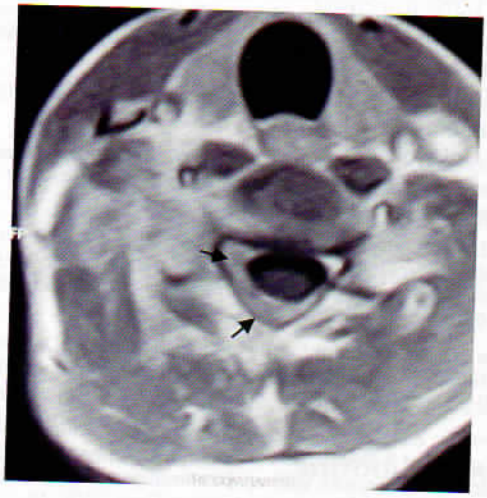

Fig. 2: Extension to spinal canal from right paravertebral region

Biopsy from the spinal lesion was attempted three times, but the reports were inconclusive. In the mean time, the patient noticed two more skin nodules over the upper limb, with rashes. Biopsy of the nodule was taken, and the histopathological report showed lymphomatous infiltration, with Non Hodgkin lymphoma, T cell type (CD3 positive). The patient was subsequently referred to an Oncology Centre for further treatment.

Discussion

About one third of non Hodgkin lymphoma cases are extra-nodal, in contrast to Hodgkin lymphoma where 80% are of nodal origin. The common extra nodal sites of involvement of NHL include the skin (cutaneous lymphoma), gastrointestinal tract, bone, testis and the nervous system.

Spinal cord lymphomas constitute about nine percent of all spinal cord tumours. Spinal cord compression as such is infrequent as a presenting symptom in patients with non Hodgkin lymphomas (NHL)[1]. Of all spinal cord lymphoma cases primary NHL producing an epidural cord compression[2] (ECC) constitutes less than three percent. A strong clinical suspicion is required for early recognition and management of the condition, which unfortunately, is often diagnosed late.

Anupam Routh[3] observed in his studies that both primary and metastatic non Hodgkin lymphoma of the spinal cord are extremely rare. Mullins, et al described only five instances of cord compression in a study of 529 cases of NHL. Their study concludes that the diagnosis is generally not suspected until a laminectomy is done.

Uncommon cases of two male patients, aged 69 and 38 years, with neurological signs as the first presenting feature of NHL were reported by Taphoorn[4]. According to him primary neurological presentation of NHL is difficult to diagnose, particularly in patients who underwent prior treatment with corticosteroids.

The most common location of epidural lymphomas is mid-thoracic spine. The clinical picture could be due to spinal cord parenchymal involvement, leptomeningeal involvement or epidural spinal cord compression. Amongst these, the commonest presentation is leptomeningeal involvement. Very rarely a compression of the peripheral nerve or nerve plexus can occur due to enlarged lymph nodes. Guillain-Barre syndrome could be a rare manifestation of lymphomas, particularly Hodgkin lymphoma. Also neurological sequelae could result from specific aggressive treatment, and include chemotherapy induced polyradiculopathy and radiation myelopathy.

Spinal cord compression is usually due to infiltration into the epidural space, which can be primary or metastatic. Primary epidural lymphomas originate from the richly vascularized mesenchymal tissues in the epidural space, adjoining bone or connective tissue. These have a better prognosis compared to metastatic lymphomas in the epidural space. Most of these lymphomas are intermediate or high grade. Quite often they are in the advanced stages and carry a bad prognosis. Histologically majority of these are histiocytic lymphomas.

Histologically about 85 - 90% of the spinal non Hodgkin lymphomas are B cell subtypes and 10 - 15% are T cell subtypes. To determine the frequency and pattern of the neurological complications of T-cell lymphoma (TCL), David K Kaufman, et al[5] had retrospectively reviewed the medical records of 316 patients with TCL diagnosed between January 1984 and May 1991. Cases were classified as having direct complications (parenchymal, leptomeningeal, epidural,

or peripheral) or indirect complications (paraneoplastic, disease related, or treatment related). The overall rate of neurological complications was 7.9%. The frequency of neurological complications in peripheral TCL and cutaneous TCL was 17% and 3%, respectively, with at least half of the neurological complications in both conditions due to direct involvement of the nervous system. Direct neurological complications of TCL were primarily due to leptomeningeal and parenchymal involvement. There were no cases of epidural spinal cord disease in their study.

Very little is known about the cellular or molecular interactions that facilitate trafficking of lymphoma cells into the CNS. Some clues are provided by a study of T-cell lymphoma with a high rate of extranodal involvement[6]. These malignancies typically stain positively with a monoclonal antibody for CD56, the neuronal cell adhesion molecule (NCAM). NCAM is a member of the immunoglobulin super-family of the cell adhesion molecules; it exhibits homophilic binding which allows NCAM molecules to facilitate adhesion among neighbouring cells with surface NCAM expression. NCAM is naturally expressed in multiple cell types in the brain, spinal cord, muscles and haematopoietic tissues.

G Székely, et al examined the course of the disease of malignant lymphoma (ML) presenting in the epidural area of the spine, in a retrospective study of thirteen patients[7]. The epidural presentation in eight patients was heralded by motor signs (paraparesis and plegia), in one by a lesion of the posterior column of spinal cord (ataxia), and in three by pain. One patient was free of complaints and symptoms. They recommended surgical intervention in nine out of the thirteen cases (seven Hodgkin and six non Hodgkin) cases. The decompression operations for tumours resulted in limited improvement in seven patients. Four patients were not operated on, two of which had significant improvement in their neurological symptoms by conservative management. The authors emphasized the importance of interdisciplinary consultation and weighing individual priorities in the indications for operation on epidural ML.

S I Landan, et al reported the incidence of syringomyelia involving the entire spinal cord[8] secondary to a spinal intramedullary tumour. Cerebrospinal fluid cytology and microscopic evaluation of gross necropsy specimens revealed a primary large cell lymphoma. Also there was massive leptomeningeal lymphomatosis involving the cortex, brainstem and cerebellum.

Conclusion

Epidural non Hodgkin lymphomas, whether primary or metastatic, are rare and are predominantly of B cell origin. In our patient, the spinal cord involvement was probably secondary, as he had evidence of skin involvement also, in the form of nodules at multiple sites. Neurological symptoms as the initial complaint of the patient, spinal cord compression from an epidural lesion as the clinical presentation, the cervical location of the tumour and T-cell origin of cells in this patient seem very rare and rather unusual, compared to the usual reported cases of non Hodgkin lymphoma.

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✪ CASE SERIES ARTICLE

Anomalous arteries in the upper limbs of a cadaver

Part I - Bilateral superficial brachioradial arteries

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Abstract

We observed a number of very unusual variations in the upper limb arteries, differing on the right and left sides, in a male cadaver in the dissection hall. The variations observed were many and are hence presented as a series, in four parts. The first part studies the variations in the axillary and brachial arteries of the two sides, with superficial brachioradial arteries bilaterally. The second part of the article describes the branches of the brachial arteries on the two sides, specially focusing on the double arteria profunda brachii and an extremely unusual anastomosis around the elbow joint. The third part deals with variations in the arteries of the left forearm and the palm of left hand, with a prominent arteria nervi mediana taking part in the formation of the superficial palmar arch. The clinical significance of all these anomalies has also been considered at length in the last part of this series article.

The right axillary artery was seen to give origin to a superficial brachioradial artery, three centimetres proximal to the lower border of teres major muscle. On the left side the superficial brachioradial artery was given off from the brachial artery, eight centimetres distal to the lower border of teres major. The branching pattern of the axillary and brachial arteries showed gross differences on the two sides. The main arterial trunk on both sides continued down the arm as brachial artery; it was seen to give off the common interosseous artery in the cubital fossa, and then continue as the ulnar artery into the forearm. All the above variations in the axillary, brachial and forearm arteries, which differed on the two sides, could be explained on the basis of the development of the upper limb arteries in the embryonic stage.

Key words: Axillary artery, Brachial artery, Superficial brachioradial artery, Double profunda brachii, Teres major muscle

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Introduction

The principal artery of arm, the axillary artery, is the continuation of the subclavian artery from the outer border of first rib. It is divided into three parts by the pectoralis minor muscle, the first part lying proximal to, the second part behind, and the third part distal to the muscle. It normally gives off six branches, the superior thoracic artery from the first part, the thoraco-acromial and lateral thoracic arteries from the second part, and the subscapular and anterior and posterior circumflex humeral arteries from the third part. Its continuation, from the level of lower border of teres major, the brachial artery, gives off an arteria profunda brachii, superior and inferior ulnar collateral arteries, nutrient branch to humerus and muscular branches. At the level of the neck of radius the brachial artery terminates by dividing into radial and ulnar arteries.

Materials and methods

The arterial variations were observed during the routine student dissection of a male cadaver in the Department of Anatomy, Pushpagiri Medical College, Tiruvalla, Kerala. The branches of the arteries of both upper limbs were traced carefully up to their termination, comparing the two sides and photographs were taken. A specific correlation of the observed variations with the embryonic development of the arteries of the upper limb is also made.

Observations

In the present study, out of the 80 upper limb specimens that had been dissected in the past few years, only one case of such wide variations in the branching pattern of upper limb arteries was observed, which in peculiar differed on the two sides. The cadaver was that of a male, aged 48 years, with a heavy build and very prominent musculature; all his blood vessels seemed very prominent; so also all the peripheral nerves appeared quite thick.

I. Right axillary and brachial arteries

The third part of axillary artery (Fig.1) was seen to give off a ***right brachioradial artery*** three centimetres above the lower border of teres major muscle. The superior thoracic and acromiothoracic arteries were seen arising from the first and second parts of the axillary artery, as usual. Just below the level of origin of brachioradial artery, the lateral thoracic artery, and one centimetre further distal to it, the subscapular and anterior circumflex humeral arteries arose from the axillary artery.

About six centimetres further distally the posterior circumflex humeral artery and two separate arteries accompanying the radial nerve in the radial groove (arteria profunda brachii) were seen to be given off as a common trunk from the right brachial artery. The posterior circumflex was unusually large and was seen to ascend towards the neck of humerus. The two profunda brachii arteries accompanied the radial nerve, one on its either side. After giving off the superior and inferior ulnar collateral branches the brachial artery entered the forearm.

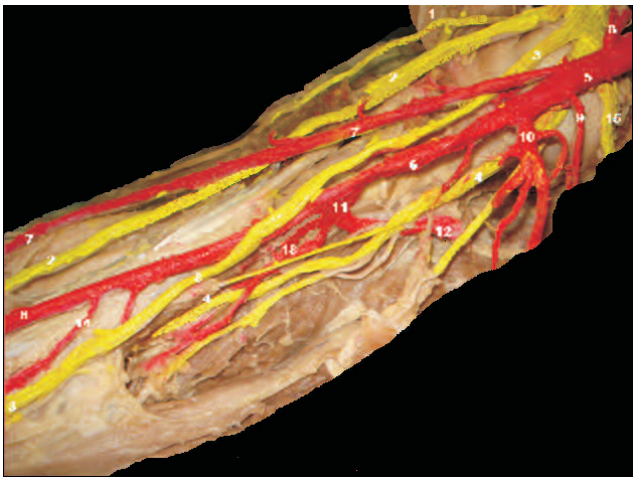

Fig.1: Right axillary & brachial arteries: relations & branches

1. Pectoralis major
2. Median N.
3. Ulnar N.
4. Radial N.
5. Axillary A.
6. Brachial A.
7. Brachioradial A.
8. Acromiothoracic A.
9. Lateral thoracic A.
10. Subscapular A.
11. Common trunk of 12 & 13
12. Posterior circumflex humeral A.
13. Double profunda brachii A.
14. Superior ulnar collateral A.
15. Axillary N.

Relation of major nerves of right arm to the arteries:

a. *Brachioradial artery* crossed *ulnar and median* nerves, from medial to lateral, superficial to both.

b. At the junction of upper and middle thirds of arm *ulnar nerve* crossed *brachial artery* from lateral to medial side superficial to it and pierced the medial intermuscular septum to descend behind the medial epicondyle. M*edian nerve* also crossed brachial artery likewise, at the level of the inter-epicondylar line of humerus. R*adial nerve* descended normally, passing posteriorly between the two profunda brachii arteries in the spiral groove.

II. Left axillary and brachial arteries

The left axillary artery was normal in length and calibre; only its third part showed anomalous branching. Anterior circumflex humeral artery was given off from the subscapular artery; posterior circumflex humeral was not seen to arise from the left axillary artery.

The ***left brachioradial artery*** was found to be given off from the brachial artery at a lower level compared to the right, 8.5 cm below the lower border of teres major; it gave no named branches in the arm. The first branch given off from the brachial artery (Fig. 2) was a common trunk dividing into posterior circumflex humeral and arteria profunda brachii. The second profunda brachii artery, originated one centimetre below the first. The superior ulnar collateral artery was seen to arise from the brachial artery opposite the origin of brachioradial; the inferior ulnar collateral branch was given off six centimetres distal to the superior branch.

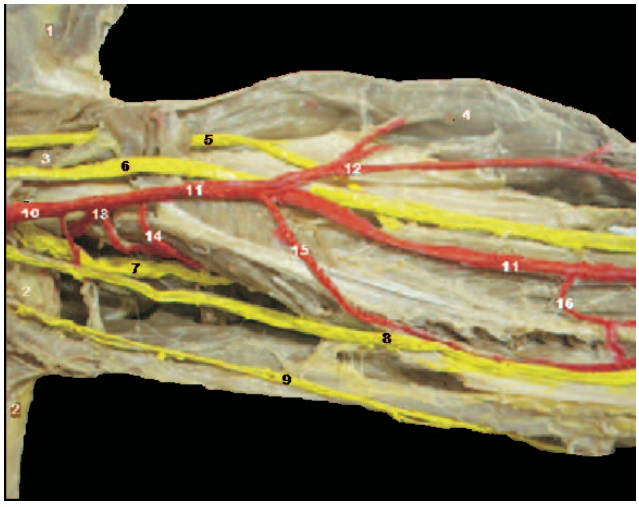

Fig.2: Left axillary & brachial arteries: relations & branches

1. Pectoralis major
2. Teres major
3. Coracobrachialis
4. Biceps brachii
5. Musculocutaneous N.
6. Median N.
7. Radial N.
8. Ulnar N.
9. Medial cut. N. of forearm
10. Axillary A.
11. Brachial A.
12. Brachioradial A.
13. Common stem of postr circumflex & 1st profunda brachii
14. 2nd profunda brachii
15. Supr. ulnar collateral A.
16. Infr ulnar collateral A.

Relation of the nerves of the left arm to the arteries:

a. *The brachioradial artery* crossed the *median nerve* superficial to it from the medial to the lateral side at the close to its origin.

b. The *ulnar nerve* was seen to lie medial to the *brachial artery* throughout its course. The median nerve descended between the brachial and brachioradial arteries in the lower part of the arm and crossed the *brachial artery* superficial to it, to reach its medial side at the level of the interepicondylar line. On the left side also the *radial nerve* was seen to descend normally, passing posteriorly between the two profunda brachii arteries.

III. Superficial brachioradial artery [branch of axillary on right side/ brachial artery on left side]

In the arm the brachioradial artery seemed much smaller than brachial artery proper, bilaterally (Fig.1 & 2). It gave no named branches in the arm other than muscular branches, and continued into the forearm deep to the bicipital aponeurosis. In the forearm it was lying superficial to the brachioradialis muscle bilaterally, and is accompanied by the superficial branch of radial nerve. Hence the artery is termed the ***superficial brachioradial artery***.

At the wrist SBR artery passed deep to the tendons of abductor pollicis longus, extensor pollicis brevis and extensor pollicis longus. The princeps pollicis and radialis indicis branches arising from the artery could be traced to their areas of supply.

On the right side a branch from princeps pollicis branch of superficial brachioradial was seen to complete the superficial palmar arch.

On the left side the superficial brachioradial artery had a small superficial palmar branch, which appeared to end supplying the thenar muscles. None of the named branches of radial artery in the palm were seen to complete the superficial palmar arch laterally on the left side. It was completed by arteria nervi mediana.

On both sides continuation of superficial brachioradial artery completed the deep palmar arch from the lateral aspect.

Discussion

Variations of the arterial patterns in the upper limb have been the subject of many anatomical studies due to their high incidence. However, many important aspects are confused due to the use of different terminologies, and different criteria for classifying them. However, such variation as in the present study, occurring at various levels in the limbs and differing on the two sides is a very rare occurence.

M Rodriguez-Niedenfuhr, et al in a detailed morphological and statistical study (Table. 1) on the variations of the arterial pattern in upper limbs, classified the different types of arterial patterns in the arm[1].

Table 1: Variation in the arteries of arm

No. of arteries	Name of arteries	Percentage
1 artery	Brachial	76.06
	Superficial brachial	4.90
2 arteries	Brachial & accessory brachial	0.26
	Brachial & brachioradial	13.80
	Brachial & superficial brachioradial	0.26
	Brachial & brachioulnar	0.26
	Brachial & superficial brachioulnar	4.20
	Others	1.04

a. Brachial artery: crosses the median nerve behind it from the medial to lateral side

b. Superficial brachial artery: courses in front of rather than behind the median nerve

c. Accessory brachial artery: it is the coexistence of two brachial arteries that rejoin before branching into the antebrachial arteries

d. Brachioradial artery (BR): high origin of radial artery coexisting with a brachial or superficial brachial artery, that branches into an ulnar artery and a common interosseous trunk.

e. Superficial brachioradial artery (SBR): is BR coursing over the brachioradialis muscle, or the tendons which define the anatomical snuff-box.

f. Brachioulnar artery (BU): a high origin of the ulnar artery coexisting with a brachial artery which branches into the radial artery and a common interosseous trunk.

g. Superficial brachioulnar artery (SBU): a brachioulnar artery coursing over the forearm flexor muscles.

h. Others include superficial brachioulnoradial artery, brachiointerosseous artery and superficial brachiomedian artery

BR originates more frequently from the brachial than the axillary artery and more specifically from the upper third of the brachial artery[1]. In the antecubital fossa, it passes posterior to bicipital aponeurosis more often than anterior to it. An artery piercing the bicipital aponeurosis has also been reported.

The superficial course of SBR may be in the proximal, middle or distal 1/3 of forearm; it usually passes through the first intermetacarpal space and ends forming the deep palmar arch[1].

In the present study the lateral branch arising from the third part of axillary artery on the right side, and the upper third of brachial artery on the left side, can be named *brachioradial artery,* as they co-exist with a brachial artery, which in the forearm divides into ulnar and common interosseous arteries. Also it can be considered *superficial* due to the following two reasons:

I. In the arm it lies superficial to the ulnar and median nerves.

ii. In the forearm it descends superficial to the brachioradialis muscle and is accompanied by the superficial branch of radial nerve.

Hence the pattern of arteries in the both study specimens is ***brachial and superficial brachioradial***. It is the most common variation of upper limb arteries (Tab. 1), more frequent unilaterally than bilaterally.

Similar cases of high division of axillary artery or brachial artery into terminal branches have been reported by many anatomists, radiologists and vascular surgeons[2,3]. Sargon M and Celik H H reported a case of high origin of radial artery from axillary, and common interosseous artery from the brachial artery (brachio-interosseous)[4] in another observation.

Sargon MF and associates reported a high origin of radial artery from the medial side of brachial artery[5]; it crossed the brachial artery laterally at a lower level. The brachial artery here ended one cm distal to the elbow joint by dividing into the ulnar, anterior interosseous and posterior interosseous arteries; the common interosseous artery was absent.

A review of 100 upper extremity arteriograms[6] showed variations in nine percent of patients. High origin of the radial artery from the brachial artery accounted for 78% of all anatomic variations. Origin of the radial artery from the axillary artery occurred only in two percent of extremities.

The superficial brachial artery reportedly divided into superficial radial and superficial ulnar arteries[7], in one limb only, in a study of 68 specimens. All the arteries coursed distally superficial to the muscles but deep to the deep fascia.

Developmental correlation

In the upper limb bud, normally only one arterial trunk, the subclavian artery persists; it is the lateral branch of the seventh cervical intersegmental artery[8]. Its main continuation to the upper limb forms the axillary and brachial arteries; it terminates as a deep arterial plexus in the developing hand. The persistent part of the artery in the forearm and hand in later life forms the anterior interosseous artery and the deep palmar arch. A branch from the main arterial trunk passes dorsally as posterior interosseous artery. Another branch accompanies the median nerve into the hand, ending in a superficial capillary plexus.

The radial and ulnar arteries appear later in the forearm. Initially the radial artery arises more proximally than ulnar and crosses in front of the median nerve. On reaching the hand ulnar artery links up with the superficial palmar capillary plexus, from which the superficial palmar arch is derived. Commonly the median artery loses its distal connection and is reduced to a small vessel.

Ontogeny:

Arey (1957)[9] is of the view that anomalous blood vessels could be developing in any one of the following manners:

a) unusual paths in primitive vascular plexuses
b) persistence of vessels normally obliterated
c) disappearance of vessels normally retained
d) incomplete development
e) fusion and absorption of parts usually distinct

The ontogenic basis of the present study of upper limb arteries can be explained correlating with the ***Singer staging of development***[10].

Stage I: Subclavian artery extends to the wrist; its distal portion forms the anterior interosseous artery

Stage II: Median artery arises from the anterior interosseous artery, and fuses with its lower portion forming deep palmar arch

Stage III: In an 18 mm embryo, ulnar arises from the brachial; it unites distally with median artery forming superficial arch

Stage IV: In a 21 mm embryo, the superficial brachial artery develops in axilla and passes down to the posterior surface of the wrist

Stage V: Median artery retrogresses, becoming the arteria nervi mediana. The distal branch of the superficial brachial artery anastomoses with the superficial palmar arch already present. At the elbow an anastomotic branch between the brachial and SB arteries forms radial artery, and the proximal portion of superficial brachial artery atrophies.

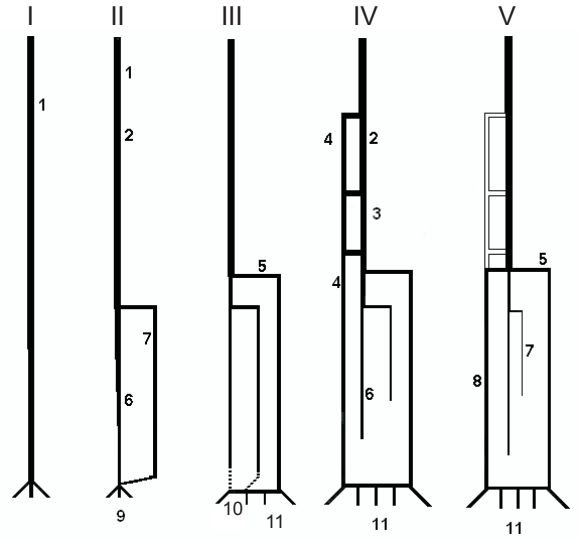

Fig.3: Singer stages of development of upper limb arteries

1. Subclavian a.
2. Axillary a.
3. Brachial a.
4. Superficial brachial a.
5. Ulnar a.
6. Anterior interosseous a.
7. Median a.
8. Radial a.
9. Deep capillary plexus
10. Deep palmararch
11. Superficial palmar arch

Melling M et al[11] suggested the development from eighth cervical intersegmental artery as an explanation for SB artery.

Rodríguez-Baeza A et al (1995) interpreted the normal development in a slightly different way[12]. According to them superficial brachial artery is a consistent embryonic vessel having two terminal branches: a medial one that divides into median and ulnar, and a lateral one which forms part of the definitive radial artery. Each of these anastomosing with a corresponding branch of primitive axial artery forms the trunks of deep origin.

In ***the present study*** the trunk of deep origin of radial artery failed to develop, or failed to attain haemodynamic predominance; hence the lateral branch, the superficial brachial artery continued as the radial artery. So also the poor development of the trunk of deep origin of ulnar artery (from the primitive axis artery) resulted in the ulnar artery seeming to be the direct continuation of brachial artery. The common interosseous artery was seen arising as its branch.

The ***different levels of origin of SBR arteries on the two sides*** can also be explained from Fig.6. Rather than one specific origin, the SBR probably had multiple sprouts from axillary/ brachial artery, some of which ultimately got obliterated and some persisted. In the present study, on the right side the branch from the axillary artery could have remained as the SBR, and on the left side a branch from the brachial artery could have persisted. Both of them extended down into the forearm later, and eventually completed the deep palmar arch laterally.

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(To be continued)

PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

A rare case of post-abortal vaginal bleeding, Uterine arterio-venous malformation, managed by Arterial embolization

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Abstract

In this case report we are discussing about a female patient who presented to us with a heavy intractable bleeding per vaginum, following dilatation and curettage for an incomplete abortion. A provisional clinical diagnosis of gestational trophoblastic disease was made, which took a very rare twist after the completion of all the relevant radiological investigations. This was one among the rarest presentations of vaginal bleeding, a uterine arterio-venous malformation (AVM). The patient was treated by uterine artery embolization, especially because she wanted to preserve fertility.

Arterial embolization could reduce morbidity in patients with uterine AVM, who usually are poor surgical candidates because of anaemia and coagulopathies. So also hysterectomy precludes future fertility. Surgical ligation of internal iliac artery has high failure rates and prevents angiographic access to the vessel, in case embolization becomes necessary later. Embolization does not preclude surgical ligation or hysterectomy, should surgical approach become necessary at a later date.

Key words: Uterine artery, Arterio-venous malformation, Arterial embolization, Post-abortal vaginal bleeding

Introduction

Arterio-venous malformations (AVM) of uterus and pelvis are considered to be one of the rarest vascular malformations. They usually present clinically associated with uterine trauma or pregnancy, when the patient complains of intractable vaginal bleeding of seemingly unknown aetiology[1]. Till quite recently, this entity was rarely ever diagnosed. But with the current advances in the radiological investigatory tools, more and more such cases are being identified and reported. Many of these cases, which would have either ended up in hysterectomy, or develop that severe anaemia as to end fatally, or very rarely undergoes spontaneous regression, are now being managed with conservative treatment options like uterine artery embolization, progestins, etc.

We are here discussing about a patient who presented to our department in Pushpagiri Medical College Hospital with severe post-abortal vaginal bleeding.

Clinical presentation

Mrs. X was a 28 year old patient with a single live child born by caesarean section, and has a previous history of two abortions. She underwent two episodes of dilatation and curettage, the first followed an induced abortion and the second was done after a spontaneous incomplete abortion at 12 weeks of gestation; both were done at a local hospital. Following the second D and C procedure, she had profuse bleeding per vaginum, for which one unit of blood had to be transfused. A check ultrasound done after the procedure did not show any retained products of conception.

About ten days after the second D and C procedure, she had two episodes of heavy bleeding per vaginum with the passage of clots; for this she was started on oral contraceptive pills (OCP). During the course of medication also bleeding continued to persist as minimal spotting PV. The withdrawal bleed after the course of OCP was normal. After

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about 15 days, she again had another episode of heavy bleeding per vaginum with passage of clots and she was referred to Pushpagiri Medical College for expert management.

Physical examination revealed mild pallor; vital signs showed that the patient was haemodynamically stable. The uterus was found to be enlarged to eight to ten weeks size. Laboratory investigations showed Hb to be 10.7mg% and a βhCG value of 54.1 IU/ml. She was started promptly on intravenous Cefotaxime and Metronidazole. During the course of her stay in the hospital there were no further bleeding episodes.

USG showed multiple hypoechoic cystic areas predominantly in the posterior aspect of myometrium (Fig. 1). There was a diffuse increase in the vascularity showing both arterial and venous flow, with turbulent flow noted within the vessels.

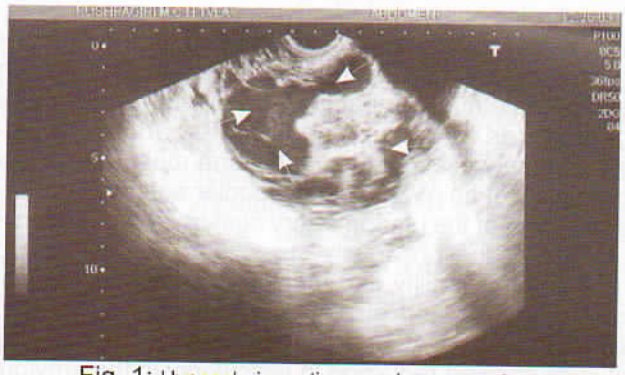

Fig. 1: Hypoechoic cystic areas in myometrium

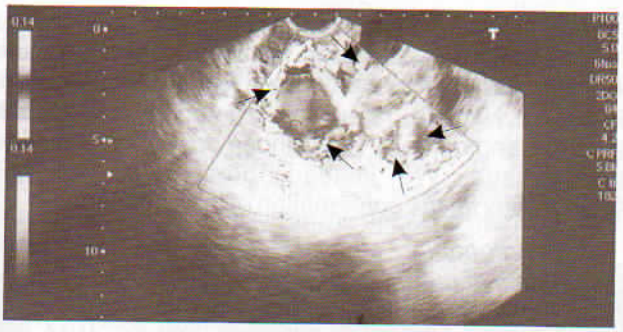

Fig. 2: Enhancement of cystic spaces with colour Doppler

The endometrial thickness measured 6.9 mm. Enhancement of the cystic spaces with Colour Doppler showed multiple engorged tortuous vessels (Fig. 2). There was no free fluid in the pouch of Douglas. MR angiogram was strongly suggested, but was not done at this stage due to non-compliance of the relatives.

On the tenth post admission day she again had a sudden onset of a heavy bout of fresh bleed per vaginum, without any associated abdominal pain. She was given intravenous Tranexamic acid as a stat dose, and was then started on oral Ethamsylate, Tranexamic acid and conjugated Oestrogen. One unit of matched red cell concentrate was also transfused. Her vital signs remained stable throughout the episode.

Once the bleeding was controlled MR angiogram of pelvis was done. It showed a bulky uterus with a large AVM involving the right uterine artery, seen in the right lateral and posterior walls of the lower part of uterine body and cervix (Fig. 3a). On the left side the AVM was seen among the branches of internal iliac artery (Fig. 4a). Irregularity of the external surface of the body of uterus was also noted.

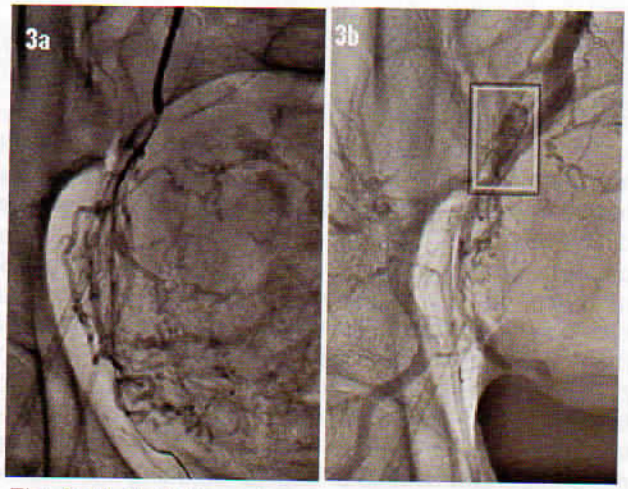

Fig. 3a & 3b: Right uterine artery before & after embolization

Elective uterine artery embolization (UAE) was done bilaterally, using Cook coil introduced into the anterior divisions of right and left internal iliac arteries (Fig. 3b, 4b). Post-embolization pictures revealed substantially reduced vascularity on both sides.

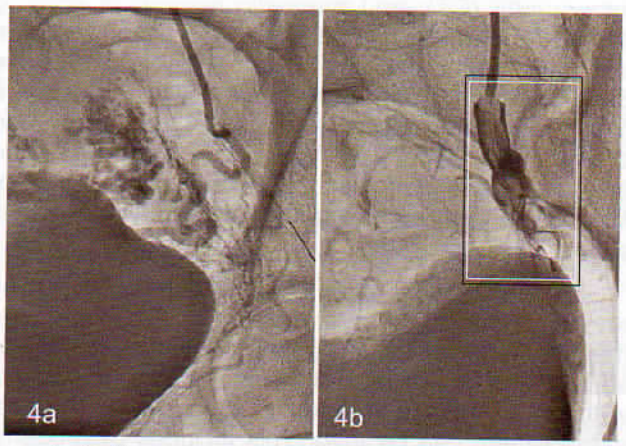

Fig. 4a & 4b: Left internal iliac artery before & after embolization

Discussion

The first case of uterine arterio-venous malformation (AVM) was reported in 1926 by Dubreuil and Loubat[2]. AVM consists of proliferation of arterial and venous channels with fistula formation and a network of small capillary like channels. In many cases, distinction between the arteries and veins becomes blurred due to secondary intimal thickening in the veins, as a result of increased intraluminal pressure. The lesion has been variably described as cirsoid aneurysm, arterio-venous

fistula, arterio-venous aneurysm, pulsating angioma, or cavernous angioma.

AVMs can be *congenital* or *acquired,* and have been reported in women aged 18 to 72 years. Most congenital uterine AVMs are isolated anomalies but can occur in association with AVM at other sites. Acquired causes[3] of uterine AVM include previous uterine surgeries like curettage, caesarean section[4] or hysterectomy, pelvic trauma[5], previous pregnancies[6], gestational trophoblastic disease[7], exposure to diethyl stilbestrol[8], endometriosis, fibromyoma, and endometrial or cervical cancers.

Anywhere in the body AVMs form a difficult task to manage, mostly because the diagnosis, prognosis, further progress and management are all clinical dilemmas. In cases of uterine AVM the clinical presentation varies from various degrees of menorrhagia to massive life-threatening vaginal bleeding. A strong clinical suspicion is essential for the prompt diagnosis and definitive treatment. Relevant previous history like any history of probable direct trauma to the uterus should be elicited. Clinical and laboratory evaluation has to be done to rule out other more important causes of vaginal bleeding like missed abortion, incomplete abortion, hydatidiform mole, dysfunctional uterine bleeding, endometrial carcinoma, polyp, etc.

In earlier days the diagnosis was usually made based on angiography[9], during laparotomy or by histopathology. With the advent of newer techniques like Colour Doppler sonography[10,11], contrast computed tomography (CT), and magnetic resonance imaging (MRI), the detection of this entity has become easier, and therefore now a days even very small AVMs are being detected. In the present day clinical practice a high index of suspicion, a good patient history and clinical examination, a falling or normal beta hCG value and the imaging studies by ultrasound Doppler or MR/ CT angiography together make the diagnosis almost 100% accurate[12].

Customarily, uterine AVM were being treated by artery ligation or hysterectomy. Presently the management depends on factors like the patient's parity status, wish for fertility and the site of AVM. In patients with less severe bleeding long term medical management can be tried. This includes oestrogens, progestins, methyl ergonovine, danazol, 15-methyl prostaglandin F_2 alpha, oral contraceptive pills, and intramuscular followed by oral methyl ergonovine maleate. Recently, Montanari and Alfie suggested the use of intravenous conjugated oestrogens and methyl ergonovine maleate combination. The authors suggested that when methyl ergonovine maleate induces tetanic myometrial contractions and thus reduces the blood flow to AVM, making it collapse, intravenous conjugated oestrogen covers the haemorrhaging vessels by proliferating endometrium. With the newer addition of uterine artery embolization into the therapeutic armamentarium, mortality fr uterine AVM could become a rare entity.

Local complications of UAE include pelvic p during embolization and in the post embolization peri neurological complications, transient butto claudication, puncture site haematoma, absce formation, vesico-vaginal fistula and endometr atrophy.

Other management modalities reported inclu laser coagulation of AVM under hysteroscopic guidan and laparoscopic coagulation of uterine arteri Hysterectomy is indicated only in those who do not wi to preserve fertility those with no access to expe medical facility or in those whom UAE fails.

In our case, the lady was referred to us with history of menorrhagia following uterine evacuation f incomplete abortion. Her initial investigations done fro the referring hospital showed minimally elevated βhC values, which were equivocal. Ultrasound study showe cystic areas in the uterine endometrium, myometriu and parametrium. At that time the differential diagnosi considered include incomplete abortion an incompletely evacuated hydatidiform mole, with a ra possibility of an AVM. Colour Doppler and further a MR angiogram of the uterine artery confirmed the presenc of AVM at the previously suspicious site. In view o retaining her fertility and menstrual functions she wa counselled for and given an option of uterine arter embolization (UAE). Post-embolization radiologica studies showed reduction in vascularity in the previous locations of AVM. She is at present kept under strict regular follow up in the OPD.

Few case reports including one from the Nagoya University Graduate School of Medicine, Showa-ku, Nagoya, Japan[13] have demonstrated the use of 3D CT angiography to diagnose post-abortal uterine haemorrhage. We instead, proceeded with MR Angiography for the confirmation of the pathology.

Pregnancy outcome after UAE for other pathologies of uterus has been reported to be positive, the commonest studied condition being fibroid uterus. The rate of pregnancy following uterine AVM can probably be increased by super-selective embolization with complete occlusion of the nidus of the malformation, preserving other pelvic branches. But as of today no statistically significant study has been reported regarding the pregnancy outcome following uterine AVM embolization.

Very few Centers have reported the successful use of embolization procedure in the treatment of uterine AVM. In Pushpagiri Obstetrics and Gynaecology Department, this is our third experience with UAE in the past two years. The first was a case of post partum hemorrhage, and the second was a case of an invasive mole with intra-peritoneal bleed. The latter patient, a nullipara, refused to undergo laparotomy and hysterectomy. All three were successfully ventured with the help of the Department of Interventional Cardiology.

Uterine artery embolization (UAE)

In the last 30 years, angiographic approach for treatment of uterine bleeding has emerged. In 1979 Brown, et al first reported uterine artery embolisation for intractable PPH. Angiographic evaluation of the bleeding vessel, and embolization with coils or gel foam or PVA (poly vinyl alcohol particles) has been established to be safe and effective. In addition to its high technical success rate, the primary advantage of angiographic embolization is preservation of fertility.

Technique:

Interestingly, embolization technique has remained largely unchanged from the initial report. In this particular case we punctured both the common femoral arteries and placed 6 French sheaths (2 mm in diameter) through the common femoral artery into the external iliac artery. Then a catheter was used to enter the opposite internal iliac artery (through the right femoral artery the catheter was negotiated retrogradely into the right common iliac artery and then across the aortic bifurcation into the left internal iliac artery and vice versa). The catheter then was negotiated into the anterior division of internal iliac artery (which supplies the uterus) and angiogram was done to evaluate the bleeders. Now 0.014" wire was introduced into the bleeding vessel and over this wire a microcatheter was negotiated into the bleeding artery. Once the micro catheter was *in situ* the embolization coils were pushed through the microcatheter into the bleeding vessel, which would thrombose and occlude the vessel. The same procedure was performed from the opposite side to embolize the right uterine artery. Once the bleeding vessels were completely embolized, the sheaths were removed and patient was shifted to CCU for overnight observation.

Usually bilateral embolization is performed, since unilateral embolization can lead to recurrence of bleed due to collaterals from the opposite uterine artery.

The agents available for embolization are gel foam cubes, or PVA particles suspended in contrast slurry. These agents cause temporary occlusion with recanalization of blood flow in 2 to 4 weeks. However in this particular situation, coil embolization was preferred, which could produce permanent occlusion of the uterine arteries, since here the bleeding was due to AV malformation, and if temporary agents are used it could lead to a recurrence of bleed.

Majority of series has reported more than 94% technical success with very few general complications like allergy to contrast and fever.

Conclusions

A strong clinical suspicion, a positive medical history, the peculiar presentation and features depicted in the radiological studies are the main features for the specific diagnosis and treatment of traumatic arterio-venous malformation resulting from uterine curettage. If diagnosed in time, and with the available facilities for conservative management by uterine artery embolization, lives can be saved in cases of bleeding uterine AVM, which is otherwise a life threatening condition. In a broad sense and generally applicable to most patients, embolization is technically achievable without major difficulties and it quickly restores haemostasis. The other specific advantage of the procedure is the preservation of fertility.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Five rare cases of peripheral artery pseudoaneurysm of upper limb

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Abstract

Pseudoaneurysm, also known as 'false aneurysm' is a haematoma that is formed as the result of leakage of blood through a defect in the arterial wall; it expands outside the arterial wall and is hence contained within the surrounding soft tissue. In other words it is a dilatation of the artery with actual disruption of only a few layers of its wall, rather than an expansion of all the wall layers. The gold standard in the treatment of pseudoaneurysm has been 'surgical' with strict adherence to the principles of vascular surgery. The repair is done with polypropelene sutures and may sometimes need a vein patch.

This article is our experience with peripheral artery pseudo aneurysms; we had five such cases involving the upper limb arteries, all managed by surgical means. The first one was on a muscular branch of brachial artery, the second in the forearm entrapping the median nerve, the third in the cubital fossa in relation to the arterio-venous fistula for haemodialysis, the fourth one was from a radial artery tributary, and the last one formed in the forearm following injury to the ulnar artery by a fracture of forearm bones. All the explorations were undertaken after Doppler evaluation, and bleeding was minimized by tourniquet control.

Key words: Aneurysm, False aneurysm, Pseudoaneurysm, Traumatic aneurysm, Peripheral arteries.

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Introduction

The term 'aneurysm' is derived from the Greek word for dilatation. It is a permanent localized dilation of artery, involving the entire weakened arterial wall, giving rise to at least 50% increase in the diameter compared to the expected normal diameter of the vessel. A pseudoaneurysm is a dilatation of the artery with actual disruption of only one or more layers of its wall (all layers not involved). Classically it arises due to partial severance of the vessel wall. The resulting haematoma is initially contained in the surrounding soft tissue and later gets walled off by the formation of a fibrous tissue sac. Since this sac lacks the elastic fibres seen in the vessel walls, continued expansion becomes unavoidable.

Clinical presentation is usually as a pulsatile mass, which is asymptomatic at the time of detection. Distal pulses are maintained and ischaemia is rarely seen, unless the sac gets thrombosed and produces distal embolization. Late presentation of such cases is usually as a pulsating mass or with features of compression on adjacent structures, palpation giving the thrill and auscultation revealing a systolic bruit. Reducibility is often not seen unless the wall is thin. The small pseudoaneurysms due to catheter related vessel wall injuries are usually asymptomatic. The definitive diagnosis is usually by ultrasound imaging, magnetic resonance angiography or CT angiography.

Clinical presentation

A brief summary of our cases of peripheral artery pseudoaneurysm is given below.

Case No. 1

A forty year old female presented with a pulsatile swelling on the antero-medial aspect of left arm (Fig. 1b) following a trivial trauma to the

site of lesion about three months back. This swelling was fusiform shaped, had 7 x 7 cm size, with transmitted pulsations palpable. It was not reducible. CT scan showed a smooth intensely enhancing lesion of size 5.7 x 4.8 cm, displacing the brachial vessels medially (Fig. 1a). The brachial vessels had normal luminal flow. A specific diagnosis of a pseudoaneurysm arising from a muscular branch of brachial artery was made. The lesion was excised (Fig. 1c) under tourniquet control.

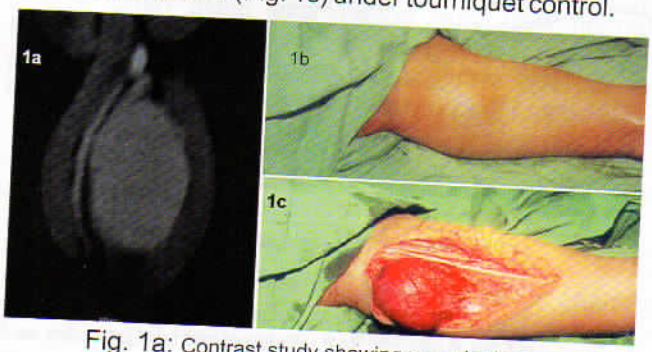


Fig. 1a: Contrast study showing vascular lesion
Fig. 1b & 1c: Fusiform aneurysm, sac exposed

Case No. 2

A forty two year old male with history of trauma to the right forearm twenty years back, presented with features of median nerve compression. He had a healed scar in the forearm and a diffuse swelling in the distal half of the forearm. This swelling was pulsatile and compressible, and a continuous bruit was heard on auscultation. Nerve conduction studies were conducted on the median nerve, which revealed a marked delay in conduction. After Doppler evaluation the forearm was explored under tourniquet control.

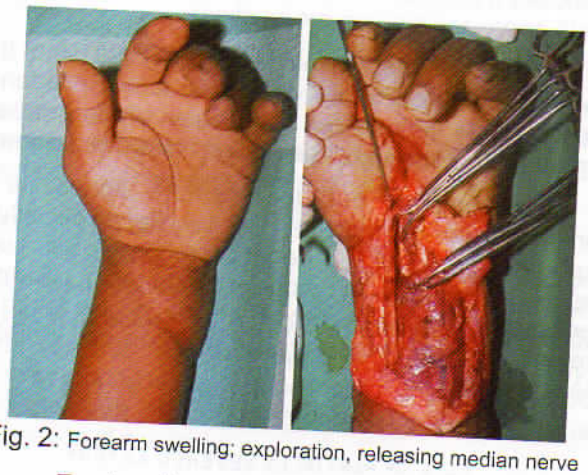


Fig. 2: Forearm swelling; exploration, releasing median nerve

Exploration revealed multiple vascular channels encasing the median nerve (Fig. 2) and the long flexor tendons. Pressure on the median nervewas responsible for the features of carpal tunnel syndrome.

Case No. 3

A twenty two year old male patient presented with a fusiform pulsatile swelling in the left cubital region; a detailed medical history revealed that he had been on maintenance haemodialysis using the left brachio-cephalic AV fistula. Two years back he had undergone renal transplantation, and since the pseudoaneurysm was now a potential focus of infection, he was advised to have it surgically removed (Fig. 3).

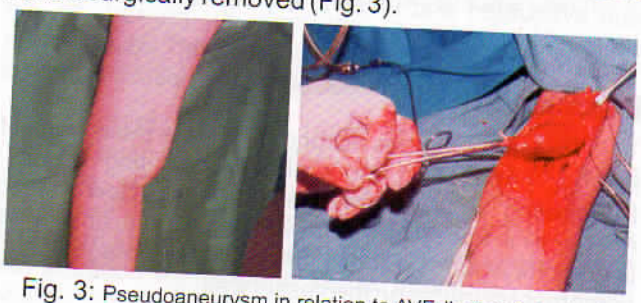


Fig. 3: Pseudoaneurysm in relation to AVF, ligated & excised

Case No. 4

A fifty one year old female patient admitted in the intensive care unit of Department of Surgery with signs of severe sepsis, showed a pulsatile swelling on her left forearm (Fig. 5). Exploration revealed the pseudoaneurysm arising from the radial artery. The feeding vessel was clamped and the radial artery continuity confirmed before closure, over a drain.

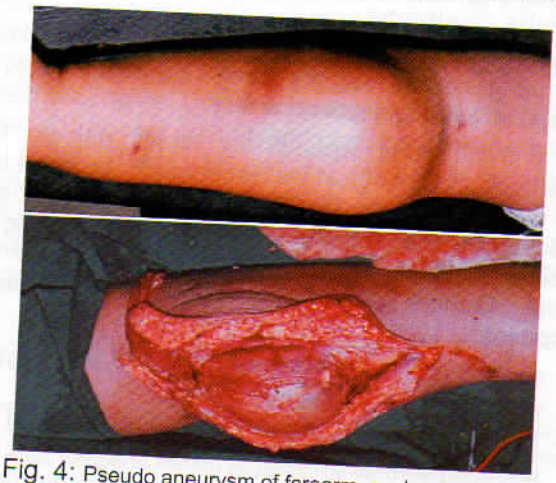


Fig. 4: Pseudo aneurysm of forearm, exploratory finding

Case No. 5

An eighty three year old female patient underwent closed reduction of fracture both bones of forearm. On removal of the cast after three weeks she showed a pulsatile swelling on the volar aspect of distal one third of forearm.

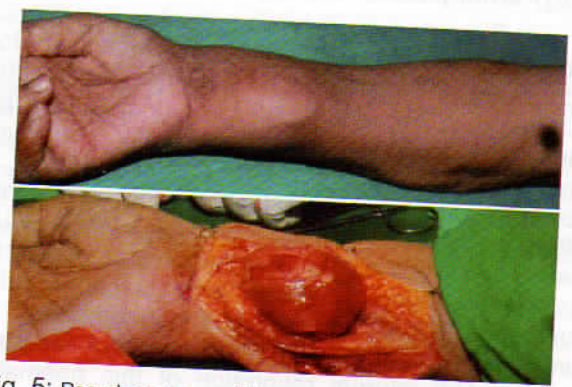


Fig. 5: Pseudoaneurysm following vessel injury by fracture

Exploration showed an organized haematoma with multiple punctures of the ulnar artery. The haematoma was evacuated and ulnar artery repair done with 8,0 ethilon (Fig. 5).

Discussion

Arterial injuries occur due to three main types of injuries: penetrating, blunt and decelerating injuries. Penetrating wounds may be either with low kinetic energy as in knife wounds or with high kinetic energy as in gunshot wounds. Blunt injuries cause damage due to compressive forces on the vessel wall.

Several parts of the arterial system are relatively fixed and hence deceleration forces produce damage at such places, the classical example being ulnar artery involvement in the Hypothenar hammer syndrome (Conn 1970)[1]. Typically this syndrome occurs in the dominant hand of persons involved in physically demanding works. The repetitive trauma to the ulnar artery in the Guyon's canal[2] leads to vessel wall damage and can present as ulnar artery thromobosis, and/ or true/ false aneurysms.

The three basic patterns of arterial damage are:

a) Completely severed artery

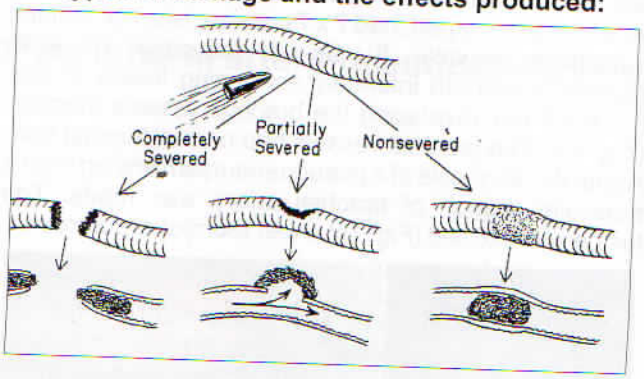
Penetrating wounds by sharp objects like knives, missiles, surgical instruments etc. produce this type of arterial injury. The severed ends constrict and retract into the adjacent soft tissue, leaving a considerable distance between the two ends of the vessel. Outline of management of such cases comprises:

- correction of hypovolaemia and shock
- wide operative exposure
- localization of site of injury, obtaining proximal and distal control
- repair of the vessel either directly or with vein grafts
- debridement and repair of other associated injuries
- prophylactic distal fasciotomy
- adequate soft tissue cover of the repaired vessel
- watch out for the maintained distal perfusion and 'reperfusion injury'

b) Partially severed artery

Severance or disruption of only a part of arterial wall is perhaps the most important arterial injury to be recognized and managed. The injury often produces recurrent bleeding and is the forerunner of both false aneurysms and arterio-venous fistulas. The partial severance seldom narrows the arterial lumen and hence the distal pulse is palpable in this type of injury. Often the injury is unrecognized and the course of events that follow is variable. Minimal wounds may heal just like the wounds that occur during diagnostic arterial punctures. A gradually expanding haematoma may form, which is contained by the adjacent soft tissues and muscle. The internal resorption of this haematoma leads to formation of a false aneurysm[3].

Types of damage and the effects produced:



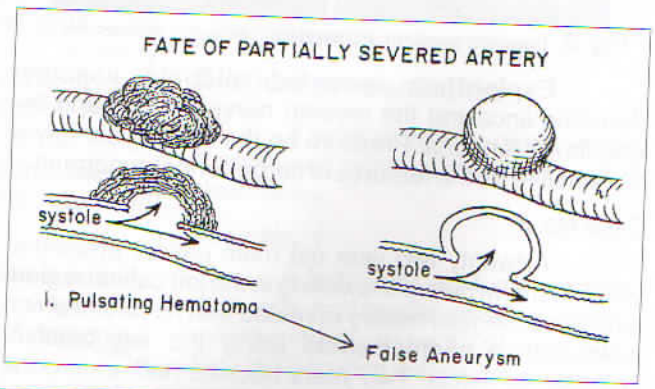
Features	Completely severed	Partially severed	Non-severed
Path-ogenesis	Ends constrict & retract	Wound gapes	Internal disruption
	Adjacent tissues compress	Adjacent tissues compress	Compression less
	Plug of clot forms, propagates	Patch of clot	Clot builds up
Result	Minimal bleeding	Minimal bleeding	Gradual occlusion
	Flow ceases	Flow persists, minimal ischaemia	No bleeding
Diagnosis	Absent pulse	H/o excessive/ recurrent bleed	Pulse disappears
	Distal ischaemia	Local findings, Angiography	Distal ischaemia

Characteristics of various types of arterial injuries

The expansile forces of the sac can produce extensile adhesions to the surrounding structures, especially if infected. An arterio-venous fistula can form if both artery and the vein are involved.

The treatment involves surgical excision of the aneurysm and restoration of arterial flow. An arterio-venous fistula is corrected by excision of the involved segments of vessels and restoration of the arterial flow.

Sometimes due to extensive adhesions a complete excision becomes impossible, especially if important structures like nerves are involved; in such cases partial wall excision is undertaken. It may necessitate a bypass also. Care has to be taken to prevent the distal emboli-zation that can occur during the procedure.



c) Non-severed artery

This is usually seen in blunt force or excess stretch to the arterial wall. Another mechanism of such injuries is the passage of a high velocity missile in the vicinity of a vessel, producing intimal damage, without actual disruption of the vessel wall. This form of injury is characterized by a reduced or absent flow through the vessel without external bleeding.

Often initial examination may give normal findings, but signs of ischaemia develop over a variable period of time. This delayed obliteration occurs due to different mechanism either alone or in combination:

a. Damaged intima leading to traumatic thrombosis
b. Sub-intimal dissection of vessel wall; intimal flap leads to luminal occlusion
c. Intramural haematoma formation

'Spasm' could rarely be a cause of arterial insufficiency. Hence in a case of suspected reduced flow, angiographic proof is often needed to differentiate spasm of circular muscles leading to reduced flow from actual intimal damage.

Evaluation and treatment

The evaluation and treatment is based on:

I. Physical examination

Look for *'soft'* signs of arterial injuries, which include history of hemorrhage or hypotension, small haematoma, adjacent nerve injury and a missile track or wound in proximity to a major vessel. The *'hard'* signs of arterial injuries include active bleeding from penetrating wound, expanding or pulsatile haematoma, bruit and thrill.

II. Doppler evaluation

Repeated clinical evaluation and Doppler are probably most useful in managing such cases. Presence of 'hard' signs and Doppler proof of arterial injury often necessitate exploration.

III. Angiography

It is used judiciously and needs to be evaluated by experienced personnel. It should not delay treatment; early exploration with evaluation of backflow from the distal cut end may give better results. A Fogarthy's catheter is used to remove the intraluminal thrombus. An intraoperative arteriogram could provide further information, if needed.

Treatment consists of surgical excision and repair of the arterial wall to restore the distal circulation. In special circumstances angiographic embolization has been tried. Sustained external compression by Doppler probe to obliterate the lumen and induce thrombosis of the sac has been reported in literature[4]. Percutaneous injection of thrombin under ultrasound guidance has also been tried and reported to be useful. These modalities of treatment are likely to be of use in simple catheter related pseudoaneurysms[5], but are unlikely to be of benefit in complex cases. Endoluminal management modalities like stent graft placement or coil embolization have also been successfully tried[6].

Surgical arterial repair is often done under magnification applying autologous vein grafts[7] or arterial conduits, which are expanded polytetrafluroethylene tubes (e-PTFE); they are used if long segments of the artery are involved. The principles of any vessel repair like irrigation with heparin saline, prevention of vessel spasm by papavarine and precisely placed non-absorbable Micro Point needle sutures go a long way in the successful outcome.

Conclusion

False aneurysms are late sequelae of partially severed vessels. Initially they present as pulsating haematomas, which eventually get fibrosed and lined by a thick sac. In this article we have tried to study five different types of peripheral arterial pseudoaneurysms which presented to our department, their different ways of presentation and the treatment adopted. Surgical repair was done under tourniquet control in all five cases. There was no intra and postoperative mortality in the study. There occurred no necessity for arterial ligation. It can be inferred that uncomplicated pseudoaneurysms managed by vascular repair[8] gives good results. Prevention of embolization and restoration of non-turbulent flow form the key to success.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Massive oedema of ovary and Polycystic ovarian disease - An uncommon association

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Abstract

A 17 year old female was admitted with severe abdominal pain and vomiting. Radiological and preoperative findings suggested a large mass arising from the pelvis, in close proximity to the right ovary. Right oophorectomy was done with a clinical diagnosis of ovarian tumour. Histopathological diagnosis was massive oedema of ovary. Peroperatively the left ovary also showed mild enlargement; hence wedge biopsy was done, and the report was polycystic ovarian disease. Massive oedema is often misdiagnosed as malignancy, and usually gets over-treated. The case is discussed here as it is a very rare association of the two pathological conditions, both being benign entities as such.

Key words: Massive ovarian oedema, Torsion, Polycystic ovary, Conservative management, Ultrasound, MRI

Introduction

Massive oedema of ovary refers to a rare tumour like enlargement of ovary, usually unilateral, due to the accumulation of oedema fluid in the stroma[1]. The condition typically occurs in young, nulliparous women. Even though it has no malignant potential, it is often misdiagnosed as a malignant ovarian tumour[2] and is usually surgically managed by oophorectomy.

Case report

A 17 year old patient was admitted with intermittent abdominal pain for the past one month and vomiting for the past two days. She gave history of irregular menstrual cycles. Per abdominal examination revealed a large cystic mass arising from the pelvis and extending up to the abdomen more towards the right side.

Investigations and management

Routine blood and urine investigation results were within normal limits. Tumour markers like CA 125, CEA, β hCG and AFP were also normal. USG abdomen and MRI scan revealed a large, predominantly cystic mass in the lower abdomen and pelvis. Uterus appeared normal. Left ovary measured 4 x 4 x 2.8 cm. Peroperatively the mass was seen to arise in close proximity to the right ovary. It appeared to have undergone torsion around a pedicle. The left ovary was also slightly enlarged. Right oophorectomy was done, along with a wedge resection of left ovary, with the provisional clinical diagnosis of malignant ovarian tumour.

Gross specimen

The right oophorectomy specimen was an enlarged ovary measuring 15 x 13 x 5 cm. The capsule was intact and its surface showed a few areas of haemorrhage (Fig. 1). Cut surface was soft and gelatinous, with multiple cystic spaces beneath the capsule, exuding clear watery fluid. The pedicle could be identified at one pole (Fig. 2). Wedge biopsy from the left ovary measured 2.5 x 1.5 cm, and showed a cortical cyst.

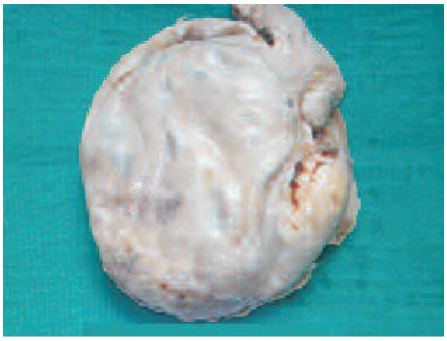

Fig. 1: Outer surface of ovary opaque, capsule intact

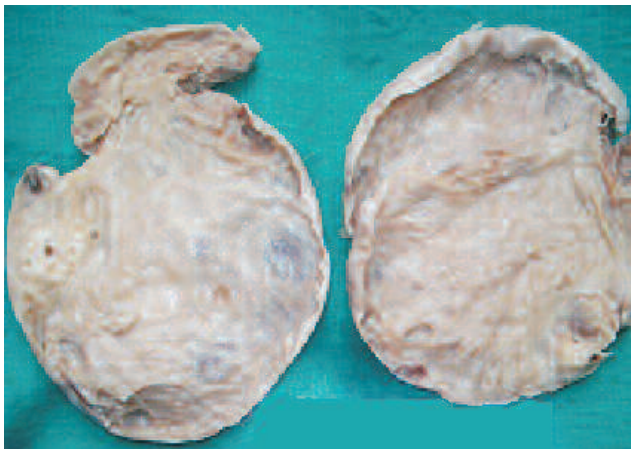

Fig. 2: Cut surface having gelatinous appearance, cysts & pedicle

Microscopy

In the right ovary cystic follicles were seen in the periphery of the lesion (Fig. 3a). Superficial cortex was thick, fibrotic and appeared as a pseudo-capsule and was not affected by the oedema (Fig. 3b). The central areas of the lesion showed marked oedema, widely separating the cells in the hypocellular stroma (Fig. 4), and surrounding the cystic follicles.

Wedge biopsy of left ovary showed follicular cysts and cortical inclusion cysts, consistent with polycystic ovarian disease.

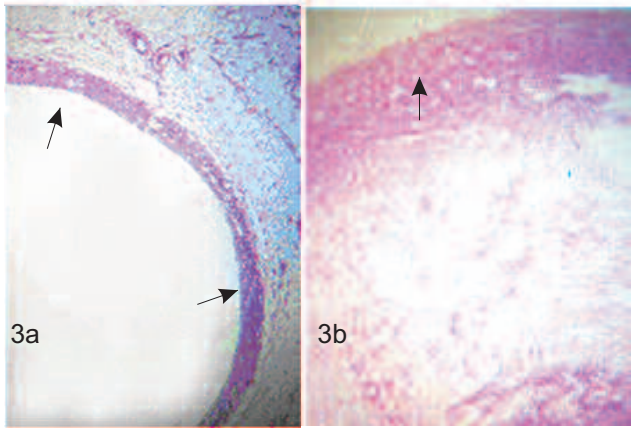

Fig. 3a: Oedema around a cystic follicle (arrows)
Fig. 3b: Thick, fibrotic cortex, uninvolved in oedema

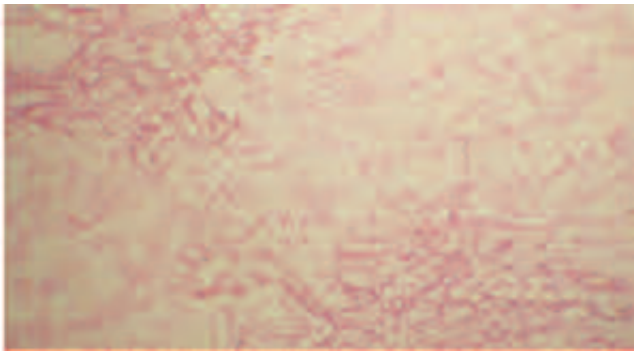

Fig. 4: Hypocellular stroma with oedema

Diagnosis:

- Massive oedema of right ovary
- Polycystic ovarian disease of left ovary

Discussion

Massive oedema of ovary is a rare tumour like entity. It was first described in the year 1969[3]. This condition is characterized by marked enlargement of one or both ovaries by accumulation of oedema fluid in the stroma, separating the normal follicular structures. It is of two types, primary and secondary[4]. In primary cases, oedema occurs in an ovary that is not diseased. But in secondary cases, massive oedema occurs in an ovary which is already diseased by conditions like malignancy, cyst, polycystic ovarian disease etc.

Our patient had unilateral massive oedema of the right ovary and evidence of polycystic ovarian disease on the left side. This could probably be a secondary massive oedema, even though we could not demonstrate any evidence of polycystic ovary in the oedematous ovary. Such an association is so rare that we could find only two similar cases[5,6] after a thorough search of the literature.

The age group affected is between six and thirty three years[7]. Most cases are around 20 years of age. About 85% of the cases are unilateral and right sided[8]. This is probably because of the high pressure in the right ovarian vein which drains directly into the inferior vena cava[9]. Left ovarian vein drains into the renal vein. Our case was also unilateral and involved the right ovary.

The exact aetiology of massive oedema is still not clear. However as there is evidence of associated torsion in about 50% of cases, it is the most widely accepted aetiologic factor. When there is complete or partial torsion of the mesovarium, there is occlusion of the venous and lymphatic drainage, which results in oedema[3]. In our case also there was evidence of torsion preoperatively. The gross specimen had a definite pedicle. Oedema causes proliferation of the stromal cells, some of which are leutinized[10] and are responsible for the androgenic manifestations in 40% of cases.

Another rare aetiologic factor is the permeation of the lymphatics by metastatic carcinomas of the uterine cervix[11], with mature cystic teratoma[12] and gastric carcinoma[13].

Most common presenting features are acute abdominal pain and a mass in the abdomen. Rare modes of presentation are menstrual irregularities, Meig's syndrome[14], precocious puberty and virilization[15].

Imaging findings in USG abdomen and MRI include a solid pelvic mass with multiple peripheral ovarian follicles[16].

Grossly the outer surface is opaque and white, with small follicular cysts beneath the cortex. The cut surface is described as watery and gelatinous.

Microscopy showed hypocellularity of the stroma in the central part due to marked oedema surrounding the follicles. Identification of cystic follicles within the oedematous tissue strongly suggests the diagnosis of massive oedema. The peripheral cortex is typically composed of dense collagenous tissue and does not participate in the oedema[3,17].

This is a condition without any malignant potential. Patients could be treated by conservative methods, or by oophorectomy. A conservative approach is considered if there is a high suspicion of massive oedema by radiological investigations. About 30% of ovarian tissue could then be removed and subjected to frozen section to exclude the secondary causes of oedema. Then untwisting of the pedicle can be done and the ovary fixed to the pelvic wall[18]. This helps in retaining the ovarian function in young females.

Conclusion

Massive oedema of ovary is a rare entity with no malignant potential. But it is often misdiagnosed as malignancy and is over treated by oophorectomy. This should always be considered in the differential diagnosis of ovarian enlargement during reproductive years. The diagnosis should be supported by the characteristic radiological findings. Every effort should be made to retain the ovarian function in the young females by a conservative approach.

The massive oedema in our case could have been secondary to the polycystic ovary, but histopathological evidence for such secondary occurrence could not be obtained.

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PUSHPAGIRI MEDICAL JOURNAL

✪ CASE REPORT

Two rare cases of recurrent subungal glomus tumour

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Abstract

This article discusses two patients who had recurrence of chronic pain in the fingertips at the subungal region. The mass at the subungal region in both cases was treated by excision and biopsy. The histopathological diagnosis was glomus tumour. Inadequate excision is usually the cause of local recurrence.

Key words: Finger, Subungal, Glomus tumour, Recurrence

Introduction

Glomus tumours are rare tumours of the hand and present with the classic triad of temperature sensitivity, severe pain and localized tenderness[1]. Normal glomus body is formed from vasculo-musculo-neuro glomus element of the nail bed, that affects regulation of blood flow[2]. The most common site of glomus tumour is in the fingers[3]. The diagnosis is often missed because of the obscurity of symptoms and the small size of the lesion.

Clinical presentation

Here we are discussing two cases of recurrence of subungal glomus tumour. Both patients were females and had complaints of pain and local tenderness. One of them had sensitivity on exposure to cold as well. The recurrences were at one year, and one and a half years after the previous excision. Both patients were treated by surgical excision by the transungal route. This was followed by meticulous nail bed repair under magnification. The symptoms disappeared totally after surgery. Further recurrence of the symptoms was not observed in the follow up for more than two years.

Representative case:

The patient was a thirty-five year old housewife. She had symptoms of pain and hypersensitivity of the nail bed of the right thumb, for which she had an excision done one year back elsewhere. There was a deformity of the ulnar side of the nail probably from the previous surgery (Fig.1b). The radiograph showed scalloping of the distal phalanx (Fig. 1a) of the thumb. Surgical excision was done by the transungal approach (Fig. 1c).

Histopathological examination confirmed the diagnosis of glomus tumour. This was followed by meticulous nail bed repair under magnification (Fig. 2a, 2b).

On follow up the patient has been symptom-free for more than two years after surgery.

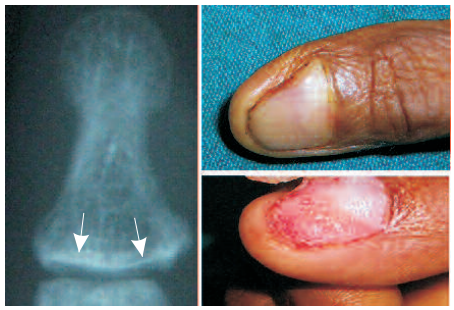

Fig. 1a: Scalloping of base of distal phalanx
Fig. 1b: Nail bed swelling - preoperative
Fig. 1c: Tumour seen through nail bed

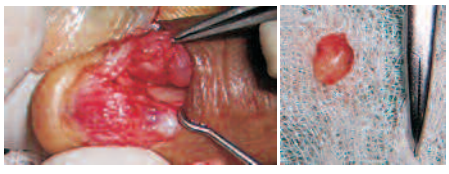

Fig. 2a: Tumour being excised
Fig. 2b: Excised tumour

Discussion

We encountered two similar cases of recurrence of chronic pain in the subungal region of fingertips diagnosted to be glomus tumour. It is a benign tumour of the neuromyoarterial glomus and the most common site is in the fingers[4]. Occasionally colour change is noticed beneath the nail and a scalloping of the distal phalanx can be seen in a radiograph[4].

The patients were treated by the transungal approach, followed by nail bed repair and repositioning of the nail. The symptoms disappeared after surgery. Surgical excision and biopsy is always necessary to confirm the diagnosis[5]. The possibility of recurrence should be emphasized upon at the time of discharge.

The common cause of a recurrence is inadequate excision; also multiple tumours must not be missed. The high resolution MRI has been useful in the diagnosis of recurrence of subungal glomus tumours, but was not applied in these two cases[3] due to financial constraints.

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PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Type 2 Diabetes Mellitus - New insights and New treatment options

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The American Association of Clinical Endocrinologists (AACE) define type 2 Diabetes Mellitus (T2DM) as "a progressive, complex metabolic disorder characterized by coexisting defects of multiple organ sites including insulin resistance in the muscle and adipose tissue, a progressive decline in the pancreatic insulin secretion, an unrestrained hepatic glucose production, and other hormonal deficiencies[1]."

Hormonal deficiencies in T2DM are related to abnormalities in the secretion of the beta-cell hormone amylin, the alpha-cell hormone glucagon, and the incretin hormones glucagon like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Other defects include accelerated gastric emptying in patients with T2DM, especially those who are obese or who have had the disease for a long duration[2].

Insulin deficiency

Impaired insulin secretion, increased hepatic glucose production and decreased peripheral glucose utilization in the muscle constitute the traditional primary defects responsible for the development and progression of type 2 diabetes mellitus.

The *San Antonio Metabolism (SAM) study 3* has established clearly that beta cell failure occurs early in the natural course of type 2 diabetes and is probably more severe than was originally appreciated. The *SAM study* demonstrated a significant marked and progressive decline in beta cell function in individuals with normal glucose tolerance (NGT). As the two-hour PG during an oral glucose tolerance test (OGTT) in NGT subjects increased from less than 100 to value ranging from 100-119 to 120-139 mg/dL, there was an associated 60% decline in beta cell function.

Ferrannini and colleagues[4] evaluated the progressive decline in beta-cell function in 188 patients with varying degrees of glucose tolerance. Patients were grouped into four categories, based on the results of an OGTT and body mass index (BMI). Lean and obese individuals with normal glucose tolerance were matched for BMI, with subjects having impaired glucose tolerance and type 2 diabetes. The results of this study showed that there was an initial increase in plasma insulin response as the PG concentration increased during the early stages of glucose intolerance. This was followed by a marked decrease in insulin levels, as the patients became more insulin resistant and hyperglycemic.

Butler and his associates[5] quantified beta cell volume in a study that analyzed pancreatic tissue from 124 autopsied individuals with varying degrees of glucose intolerance [Normal glucose tolerance (NGT), impaired glucose tolerance (IGT) and type 2 diabetes]. In patients with IGT and type 2 diabetes there was a progressive decrease in beta cell volume that was related to an increase in beta cell apoptosis. This suggests that treatment strategies for patients with type 2 diabetes should include agents that may delay and/ or prevent beta cell apoptosis.

Insulin resistance

Insulin resistance is the key pathological defect, and is a characteristic feature of type 2 diabetes (Fig.1). Both liver and muscle are severely resistant to the action of insulin. Using the gold standard euglycemic insulin clamp technique, it has been shown that skeletal muscle is severely resistant to insulin and accounts for 85 to 90% of the impairment in total body glucose disposal in patients with type 2 diabetes.

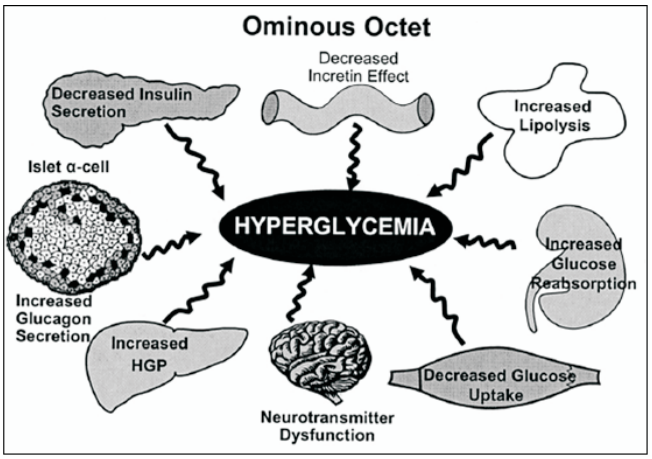

Fig1. Multiple defects contributing to the pathogenesis of diabetes

Adipocytes and Adipokines

Considerable evidence demonstrates that deranged adipocyte metabolism and altered fat topography play an important role in the pathogenesis of glucose intolerance in type 2 diabetes[6]. Fat cells are in a state of chronic inflammation and secrete excessive amounts of insulin resistance-inducing, inflammatory, and atherosclerosis-provoking cytokines (tumour necrosis factor, interleukin-6, resistin and angiotensinogen), and fail to secrete normal amounts of insulin-sensitizing adipocytokines (adiponectin). Fat cells are also resistant to the anti-lipolytic effect of insulin in type 2 diabetes, leading to elevated plasma free fatty acid (FFA) concentrations and increased levels of toxic lipid metabolites (fatty acyl coenzyme A, diacylglycerol, ceramide etc.), i.e., lipotoxicity[7]. These toxic lipid metabolites cause insulin resistance in muscle and liver, and promote beta cell failure[8].

Incretins and Glucagon

Incretin effect is the ability of oral glucose to elicit a better insulin secretion than when the same amount of glucose is given intravenously, i.e., the intestine can sense the amount of glucose in the intestine, and can secrete factors that can stimulate insulin secretion and suppress glucagon levels. Patients with type 2 diabetes have diminished incretin effect as a result of incretin hormone deficiency and/ or resistance[9]. The incretin hormones, glucagon like peptide-1(GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) account for 90% of the incretin effect and are pivotal in maintaining glucose homeostasis. Both GLP-1 and GIP augment insulin secretion. GLP-1 also inhibits glucagon secretion, delays gastric emptying, and suppresses the appetite of the patient[10].

Glucagon plays a pivotal role in the maintenance of the majority of basal hepatic glucose output in patients with type 2 diabetes. Plasma glucagon concentrations are increased in patients with impaired glucose tolerance and type 2 diabetes compared with individuals with NGT, despite hyperglycemia and hyperinsulinemia which should suppress glucagon secretion. The elevated concentrations of glucagon resulting from increased pancreatic alpha cell secretion, enhance the hepatic glucose output and aggravate the hepatic insulin resistance[11].

Glucose reabsorption in Diabetes

In patients with diabetes, it would be desirable for the kidney to excrete the excessive filtered load of glucose in an attempt to restore normoglycemia. In contrast, the diabetic kidney responds to the ambient hyperglycemia by enhancing glucose reabsorption, thereby contributing to the pathogenesis of glucose intolerance[12].

Neurotransmitter dysfunction

Neurotransmitter dysfunction in the central nervous system plays a key role in aetiology of type 2 diabetes. Under normal circumstances, insulin signals the brain to stop eating and decrease energy intake. Obese patients with and without type 2 diabetes are markedly insulin resistant, and the beta cells respond to insulin resistance with a compensatory increase in the insulin secretion. Despite hyperinsulinemia which should suppress the appetite, obese people continue to over eat, indicating that the appetite centres must be resistant to insulin; indeed, this has been demonstrated using functional magnetic resonance imaging[13].

New treatment options for Type 2 DM:

Based on the various pathophysiological mechanisms responsible for the evolution of type 2 diabetes, a review of the current therapeutic options is in order.

1. In the liver, some drugs like Metformin and Thiazolidinediones (TZDs) are potent insulin sensitizers, and inhibit the increased rate of hepatic gluconeogenesis responsible for the elevated rate of basal hepatic glucose output in patients with type 2 diabetes. In the muscle TZDs are potent insulin sensitizers, whereas metformin is a weak insulin sensitizer.

2. The *incretins (GLP1, GIP)* also have been shown to improve beta cell function and maintain the durability of glycemic control.

[**a**] *Exenatide* is a synthetic version of exendin-4, with 53% homology with native GLP-1. Administered parenterally, exenatide reduces HbA1c, increases insulin secretion, and preserves beta cell function for about 3½ years.

[**b**] *Liraglutide*, a once-daily human GLP-1 analogue, has been submitted to the US Food and Drug Administration (FDA) for approval. In a 14-week study in 39 patients with type 2 diabetes, liraglutide (0.65, 1.25, or 1.9 mg/day) produced improvements in first- and second-phase insulin secretion and in arginine-stimulated insulin secretion during hyperglycemia.

[**c**] The other incretin - based agents include the *dipeptidyl peptidase-4 (DPP-4) inhibitors like sitagliptin and vildagliptin.* They are orally administered and increase endogenous levels of GLP-1 by inhibiting the enzyme DPP-4. The increased levels of GLP-1 in turn cause increase insulin secretion from the pancreas and also suppresses glucagon secretion. Monotherapy with sitagliptin over 18 weeks resulted in a reduction in HbA1c of 0.6% from baseline compared with placebo. Of the patients receiving sitagliptin, 35.8% patients achieved seven percentage HbA1c, compared with 15.5% of patients receiving placebo.

3. SGLT-2 (Sodium Glucose Symporter-2) is mainly responsible for the reabsorption of glucose from the glomerular filtrate in the renal proximal tubule. Inhibitors of this transporter, eg., *Dapagliflozin* block glucose reabsorption and promote glycosuria, and thus lower serum glucose levels. Increased urinary glucose loss lowers serum glucose, but crucially these drugs appear to have this effect only in states of hyperglycaemia. Dapagliflozin has a half-life of approximately 17 hours, and almost a maximal SGLT-2 blockade for at least 24 hours following doses of 25–50 mg, making this suitable for once-daily dosing.

4. *Quick releasing Bromocriptine* has been used to tackle neurotransmitter dysfunction. It can decrease the levels of brain Neuropeptide Y and increase the dopamine levels in the brain, leading to reduction in the hyperphagia, and thus blood glucose levels. It can also decrease the serum lipid levels.

Ongoing research has provided more in-depth knowledge about the pathophysiology of type 2 diabetes, leading to a better understanding of the multiple defects involved in disease progression. Clinical trials, which focus only on reducing HbA1c, have demonstrated continual disease progression and eventual treatment failure. Therapy therefore should focus on delaying disease progression by targeting the pathogenic disturbances underlying type 2 diabetes (i.e., increasing insulin sensitivity and maintaining beta cell function). To achieve these goals, aggressive combination therapy should be initiated early in the natural course of the disease. Newer therapeutic options and agents in development make this therapeutic approach increasingly feasible.

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✪ TECHNICAL REPORT

Free Radicals - A general approach

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Free radicals are a chemical species that possess unpaired electrons. These electrons account for their reduced chemical stability and high reactivity. They are produced continuously within the cells. The important free radicals generated in the body are derivatives of oxygen and are termed Reactive Oxygen Species (ROS), eg. super oxide radical, hydroxyl radical, peroxy radical, hydrogen peroxide, singlet oxygen, nitric oxide radical, peroxynitrite, hypochlorous acid, etc[1].

Chemistry of free radical generation

The outermost orbital of an atom contains paired electrons, which account for its chemical stability. But loss of one electron makes it unstable and highly reactive (Fig. 1).

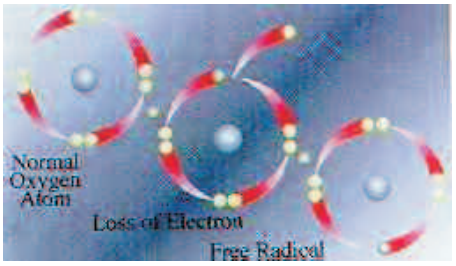


Fig. 1 Generation of an oxygen free radical

Sources of free radicals

It includes both endogenous and exogenous sources.

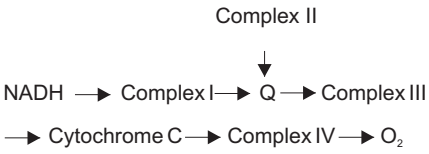
I. Endogenous sources:

They are auto-oxidation, enzymatic oxidation, respiratory burst, electron leaking of respiratory chain etc[2].

a) Auto-oxidation: of catecholamines, haemoglobin, myoglobin etc. results in the formation of reactive oxygen species[1].

b) Enzymatic oxidation: A variety of enzyme systems are capable of generating significant amounts of free radicals. They include xanthine oxidase (activated in ischemia-reperfusion injury), cyclo oxygenase (the Arachidonic acid cascade pathway), lipo-oxygenase (by Leukotriene pathway), amino acid oxidase, Cyt P^{245} NADPH oxidase (macrophages), myelo-peroxidase (in neutrophils), Cyt P^{450} mono oxygenase (detoxification)[4].

c) Electron leaking of respiratory chain: Normal electron transfer through the respiratory chain can be represented as follows:



But when electron transfer is reduced by a high membrane potential, or by respiratory inhibitors such as antimycin A, complex III may leak electrons directly to molecular oxygen without involving complex IV (Fig. 2), resulting in superoxide formation[6].

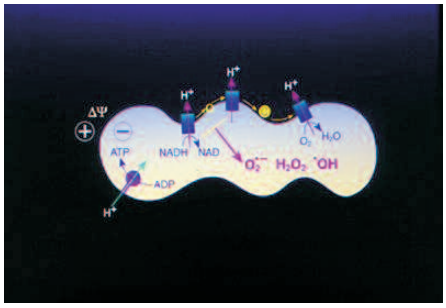


Fig. 2 Electron leaking of respiratory chain

d) Respiratory burst: This mechanism is involved in phagocytosis, and has duration of 30 to 60 minutes. During this period the consumption of oxygen by the cells is drastically increased (Fig. 3) and hence this is called respiratory burst[5]. There is a deliberate production of free radicals.

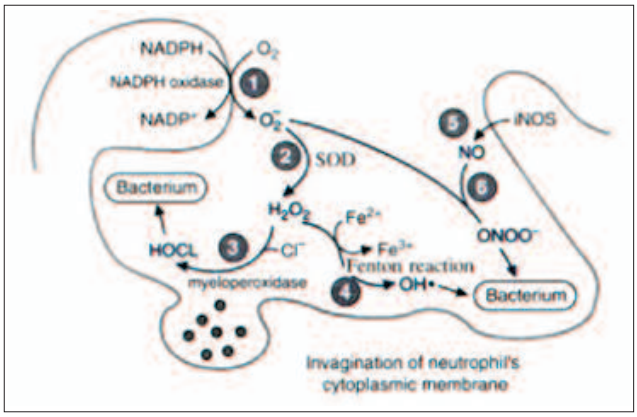


Fig. 3 Respiratory burst: deliberate production of free radicals

II. Exogenous sources

a) Drugs: anti-neoplastic agents like bleomycin, adriamycin and methotrexate, others like pencillamine, phenyl butazone etc.
b) Radiation: radiotherapy causes tissue injury by free radicals.
c) Tobacco smoking: this forms the source of a variety of free radicals; it also elevates the amount of neutrophils[7].

Mechanism of harmful effects of free radicals

- *Lipid peroxidation*: is oxidative deterioration of unsaturated or polyunsaturated fatty acids by a free radical chain reaction. This generates toxic by-products like MDA, which causes DNA damage by forming adducts with deoxyguanine[8].
- *Mitochondrial damage*: is caused by super oxide radicals generated by electron leaking of respiratory chain (Fig. 4). Due to their instability they attack DNA, membrane proteins, glutathione etc. If the damage is severe, mitochondria experience apoptosis or programmed cell death[9].

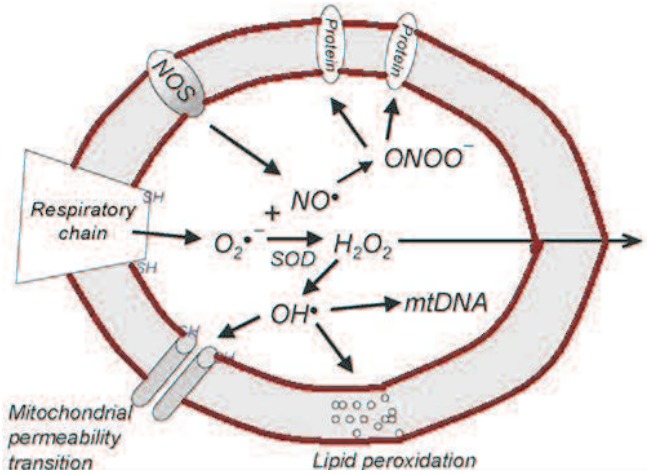


Fig. 4 Mitochondrial damage

- *DNA damage*: could be either nuclear or mitochondrial

a) Nuclear DNA damage:

Hydroxy (OH) radical reacts indiscriminately with all components of DNA by:

i. Direct interaction
ii. Stimulating the rise of extracellular Ca^{2+}: this activates endonucleases to cause strand breaks, which may be single or double (Fig. 5). This may result in multiple broken chromosomes (Fig. 6).
iii. Other forms of damage include modification of all bases, production of base free sites, deletion, frame shift, DNA - protein cross links and chromosomal rearrangement[10].

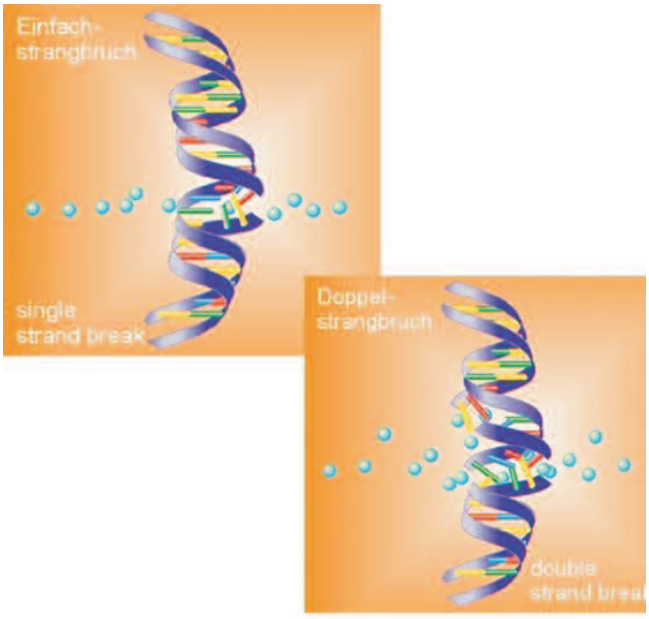


Fig. 5 Single and double strand break

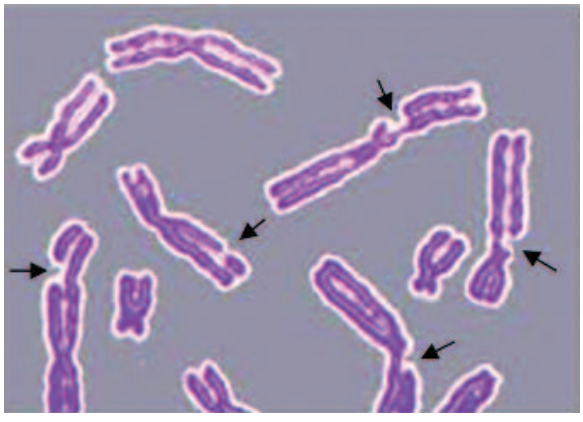


Fig. 6 Multiple broken chromosomes

b) Mitochondrial DNA damage

Mitochondrial DNA is susceptible to damage than nuclear DNA because:

I. It is not protected by histones or DNA binding proteins

ii. DNA repair mechanism is less efficient in mitochondria than in the nucleus[11].

Role of free radicals in the pathogenesis of diseases

The free radicals form an underlying cause in the pathogenesis of several disorders:

- *Ageing*

Free radicals get accumulated in mitochondria with age, and mitochondrial DNA is the primary site of radical damage. Damage progresses and shuts down mitochondrial oxidative phosphorylation, causing many cells to die and the organism to age. Wrinkle formation is mainly due to oxidative damage and decreased activity of antioxidant enzymes[12].

- *Cancer*

Free radicals are agents that promote cancer, and act by altering gene expression. This is by mobilizing calcium ion stores which activate cellular kinases, phosphatases and transcription factors. They cause gross chromosomal damage and also inhibit the DNA repair system. Lipid peroxidation is also a causative factor in cancer development[13].

- *Diabetes mellitus*

Hyperglycemia is an underlying cause for the generation of reactive oxygen species (ROS). Mechanism of generation is by the non - enzymatic glycation of proteins, amino groups of phospholipids and DNA, and also via pro-inflammatory cytokines which activate cyclo-oxygenase. Most of the complications of diabetes mellitus are due to ROS generation[14].

- *Coronary artery disorders*

The initiating step in cardiovascular diseases is endothelial damage, which exposes these lining cells and the underlying cell layers to a deleterious inflammatory process, which ultimately leads to the formation of atherosclerotic lesions[15]. Intrinsic to the development of these lesions there is cellular oxidative stress due to the production of damaging free radicals (reactive oxygen and nitrogen species) by many cell types including endothelial cells, vascular smooth muscle cells, monocytes and macrophages. Increased oxidative stress inactivates nitric oxide (anti-atherosclerotic agent) to peroxy nitrite radicals, which leads to impaired endothelial function. Further, the LDL oxidized by free radicals is phagocytosed, to give rise to foam cells and plaques, which cause thickening of the vessel wall and blockage of lumen. In myocardial ischaemia ROS are generated by xanthine oxidase, catecholamine auto-oxidation and neutrophil activation.

- *Liver diseases*

Free radicals from NADPH oxidase of macrophages in hepatic Kupffer cells play a major role in the pathogenesis of viral or alcohol induced hepatitis. Alcohol also stimulates Cyt P^{450} which is in involved ROS generation. Further, ROS activates NF - kB (transcription factor), which increases the mRNA level of TNF-alpha and IL-12 (hepatic pro-inflammatory cytokines), resulting in liver cell injury[16].

- *Lung diseases*

ROS injury of pulmonary system is due to its continuous exposure to toxic pollutants, and also due to the infiltrating neutrophils. Thromboxane (TXA2) produced from arachidonic acid (released by the neutrophils) causes vasoconstriction as well as bronchoconstriction, leading to ischaemic reperfusion injury. Xanthine oxidase induced ROS generation changes the mitochondrial functions and causes Ca^{2+} leak, and may induce apoptosis[17].

- *Infectious diseases*

ROS like nitric oxide (NO) affect host immune response by suppressing type II helper T cells, and contribute to the pathogenesis of viral infections. Super oxide and nitric oxide induce production of cytokines like IL-1beta, IL-2, IL-6 and TNF-alpha involved in viral replication and gene expression. Peroxy-nitrite formed by the action of nitric oxide synthase causes oxidative tissue injury and mutagenesis[18].

- *Inflammatory diseases*

Major causes of oxidative damage are accumulation of neutrophils in the inflamed tissues, and the superoxides generated by xanthine oxidase during ischaemia-reperfusion. These superoxides act as cellular messengers and elicit inflammatory response, and also induce gene expression encoding inflammatory proteins (eg. proteinases like collagenases and elastases), leading to tissue destruction[19].

- *Male infertility*

ROS causes:

I. Reduction in overall sperm production
ii. Loss of sperm motility due to impaired mitochondrial energy production
iii. Impairment of sperm - oocyte fusion due to loss of membrane fluidity
iv. Sperm DNA fragmentation
v. Abnormal sperm morphology
vi. Impairment of acrosome reaction mainly by lipid peroxidation[20]

- *Female infertility*

Free radicals induce inflammatory cytokines like TNF - alpha, IFN - gamma and IL - 1 involved in the various aetiologies of female infertility such as polycystic ovary syndrome, endometriosis, tubal

obstruction, pre-eclampsia, birth defects and recurrent abortions[21].

- *Neurological disorders*

i. Parkinson's disease: H_2O_2 produced by mono amino oxidase (MAO) during the turnover of dopamine is implicated in the pathogenesis of the disease. Hydroxyl (OH) radicals from H_2O_2 cause damage to the neurons.

ii. Down syndrome: results by trisomy of chromosome 21, which also encodes SOD leading to the generation of H_2O_2 and OH radicals.

iii. Alzheimer's disease: oxidative damage to different biomolecular components of brain is linked to the pathophysiology of AD[22].

How are the free radicals formed in the body eradicated?

Antioxidant system is the body's defence mechanism against free radicals. They are substances that protect vital molecules from the damaging reactions of reactive oxygen species by interacting with them. These include enzymes like super oxide dismutase, catalase, glutathione peroxidase and also vitamins like ascorbic acid, beta-carotene and alpha tocopherol[23].

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PUSHPAGIRI MEDICAL JOURNAL

✪ TECHNICAL REPORT

Nanoparticle-based drug delivery systems: A mini review

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Abstract

Over the past three decades, there has been considerable research interest in the area of developing drug delivery using polymeric nanoparticles (NPs) as carriers for small and large molecules. Targeting delivery of drugs to the diseased lesions is one of the most important aspects of drug delivery system. They have been used *in vivo* to protect the drug entity in the systemic circulation, to restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to the site of action. Various polymers have been used in the formulation of nanoparticles for drug delivery research to increase their therapeutic benefit, while minimizing the side effects. Nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. The current review briefly mentions the methods of preparation of nanoparticles, their physico-chemical characterization, targeted release and the applications in the delivery of drug/ gene/ protein molecules.

Introduction

Nanotechnology is a science of atomic scale phenomenon and mostly deals with particles ranging from 100 nm to 0.1nm. It has now become possible to handle individual atoms, pick them up or place them shifting from one place to another. The nanoparticles have endless applications including drug, gene and protein delivery. The drug/ DNA/ protein can be dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Based on the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. This multidisciplinary scientific field involves creation and utilization of materials, devices or systems, which have enabled the development of an amazing variety of methods for fabricating nanoparticles in the recent years. This technology is equally innovative and has a critical role in the controlled release of drugs.

In recent years, biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymers such as poly ethylene glycol (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time targeting a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes[1,2,3,4] .The development of a wide spectrum of nanoscale technologies is beginning to change the foundations of diagnosis, treatment, and prevention of diseases. These technological innovations, referred to as the nano-medicines by the National Institutes of Health (Bethesda, MD, USA), have the potential to turn the molecular discoveries arising from genomics and proteomics into widespread benefit for patients.

The major goals in designing nanoparticles as a delivery system are to control the particle size, surface properties and the release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. Research into the rational delivery and targeting of the pharmaceutical, therapeutic, and diagnostic agents is at the forefront in nanomedicine. These involve the identification of precise targets (cells and receptors) related to specific clinical conditions and choice of the appropriate nanocarriers to achieve the required responses while

minimizing the side effects.

Though liposomes have been used as potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and dose reduction, their applications are limited due to inherent problems such as low encapsulation efficiency, rapid leakage of water-soluble drugs in the presence of blood components and poor storage stability. On the other hand, polymeric nanoparticles offer some specific advantages over liposomes. For instance, they help to increase the stability of drugs/ proteins and possess useful controlled release properties[5,6,7]. The advantages of using nanoparticles as a drug delivery system include the following:

1. Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.

2. They control and sustain the release of drugs during their transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.

3. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity.

4. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.

5. The system can be used for various routes of administration for drugs including oral, nasal, parenteral, intra-ocular etc.

In spite of these advantages, nanoparticles do have limitations. For example, their small size and large surface area can lead to particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms. In addition, small particles size and large surface area readily result in limited drug loading and burst release. These practical problems have to be overcome before nanoparticles can be used clinically or made commercially available.

Preparation of Nanoparticles

Nanoparticles have been prepared most frequently by three methods: (1) the dispersion of preformed polymers; (2) polymerization of monomers; and (3) ionic gelation or coacervation of hydrophilic polymers. Nanoparticles can be prepared from a variety of chemical substances such as proteins, polysaccharides and polymers. The selection of matrix materials is dependent on many factors[8] including: (a) size of nanoparticles required (b) inherent properties of the drug (c) surface characteristics such as charge and permeability (d) the extent of biodegradability, biocompatibility and toxicity (e) drug release profile desired and (f) antigenicity of the final product.

Effect of characteristics of Nanoparticles on drug/ protein delivery

Particle size and distribution are the most important characteristics of nanoparticle systems. They determine the *in vivo* distribution, biological fate, toxicity and the targeting ability of nanoparticle systems. In addition, they can also influence the drug/ protein loading, drug/ protein release and the stability of the nanoparticles. Many studies have demonstrated that nanoparticles of sub-micron size have a number of advantages over microparticles as a drug delivery system[9]. Generally nanoparticles have relatively higher intracellular uptake compared to microparticles and become available to a wider range of biological targets due to their small size and relative mobility. Drug release is affected to a great extent by the particle size. Smaller particles have larger surface area, and therefore, most of the associated drug would be at or near the particle surface, leading to faster drug release. On the other hand, large particles have larger cores which allow more drug to be encapsulated and they diffuse out slowly[10]. Smaller nanoparticles also have greater risk of aggregation of particles during storage, transportation and dispersion. It is always a challenge to formulate nanoparticles with the smallest size possible but maximum stability. Degradation of the polymers is also affected by the particle size.

The zeta potential is commonly used to characterize the surface charge property of nanoparticles[11]. It reflects the electrical potential of particles, and is influenced by the composition of the particle and the medium in which it is dispersed. Nanoparticles with a zeta potential above (+/-) 30 mV have been shown to be stable in suspension, as the surface charge prevents aggregation of the particles. The zeta potential can also be used to determine whether a charged active material is encapsulated within the centre of the nanocapsule or adsorbed onto the surface.

The most promising area of the application of polymeirc nanoparticles seems to be their use as parenteral carriers for different drugs. They are used in various purposes like tumour-targeting drug delivery, oral delivery of peptides and proteins, targeting to epithelial cells in the GI tract using certain ligands, gene delivery applications, drug delivery to the brain crossing blood-brain barrier, etc. A number of authors have demonstrated a considerable tendency for an accumulation of polymeric nanoparticles in certain tumours. The binding of a variety of cytostatic drugs like 5-fluorouracil, Paclitaxel[12] and Doxorubicin[13,14] to albumin or gelatin nanoparticles significantly enhanced their efficacy in experimental tumours or human tumours transplanted to nude mice, in comparison with the free drug. Moreover, the toxicity of Doxorubicin was substantially reduced by binding to nanoparticles.

Gelatin nanoparticles are used as immunological adjuvants to enhance both the humoral and the cellular responses to antigens[15,16]. Many researchers have used gelatin nanoparticles as gene delivery vehicle[17].

Conclusion

Polymeric nanoparticles hold promise as drug delivery systems for parentral, peroral and ocular administration as well as an adjuvant for vaccines. Due to their greater stability and easier manufacturing techniques they offer advantages over other colloidal carriers such as liposomes and cell ghosts. The physico-chemical properties of the drugs play an important role in the choice of the nanoparticle material that has to be employed. Other advances are required in order to turn the concept of nanoparticle technology into a realistic practical application as the next generation of drug delivery system. It can be anticipated that where large scale fabrication of such nanoparticles is successful, the application of such delivery systems in nanobiotechnology will contribute to de-bottlenecking of current biopharmaceutical manufacture.

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✪ TECHNICAL REPORT

Clinical approach to Metabolic Acidosis

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In this article the salient points on the approach to metabolic acidosis in adults are discussed. Mixed acid disturbances are not discussed here. So also a detailed elaboration of each aspect with the mechanisms and treatment modalities is beyond the scope of this article.

In the body there is a constant production of carbonic acid as well as non-volatile acids, by metabolic processes. These must be eliminated in order to keep the pH of the body fluids in the normal range. CO_2 is produced to the tune of 15,000 mmol/day and the non-volatile acids (predominantly H_2SO_4) to the tune of 50 to100 mmol/day. This acid load has to be eliminated by lung as well as kidney.

The pH of body fluids normally is 7.4 ± 0.05. The pH can be expressed by the well known equation, Henderson-Hasselbach equation:

$$pH = 6.10 + \log [HCO_3] \div [0.03 \times pCO_2]$$

where 6.1 is the pKa of the carbonic acid system, 0.3 is the solubility constant for CO_2, and pCO_2 is the partial pressure of CO_2.

Metabolic acidosis is defined as low arterial pH and low bicarbonate level. It can be produced by:

A. Increased generation of acid
B. Loss of bicarbonate
C. Failure of excretion of H^+ ions

A. Increased generation of acid occurs in a variety of conditions:

1. Lactic acidosis
2. Ketoacidosis due to uncontrolled diabetes mellitus, excess alcohol intake, or fasting
3. Ingestions: methanol or ethylene glycol, aspirin, toluene
4. Increased retention of acid as occurs in renal failure
5. D-lactic acidosis

B. Increased loss of bicarbonate occurs in two settings:

1. Loss of bicarbonate in diarrhoea
2. Loss of bicarbonate through kidney in proximal renal tubular acidosis

C. Failure of excretion of acid load by the kidney occurs in two settings:

1. Renal failure
2. In Distal RTA (type I)

In the differential diagnosis of metabolic acidosis it is very useful to categorize the causes into two groups, one with high anion gap (High Anion Gap Metabolic Acidosis - HAGMA), and another with normal anion gap (Normal Anion Gap Metabolic Acidosis - NAGMA).

Anion gap (AG) is defined as the difference between measured cation (Na) and the sum of the measured anions ($Cl + HCO_3$).

$$\text{Serum AG} = Na - (Cl + HCO_3)$$

Normal Anion Gap = 140 – (104 + 24) = 12 meq/L (12 ± 4). Some physicians include potassium also. If it is included, the normal Anion gap is increased by 4 meq/L.

Serum AG is primarily determined by negative charges on serum proteins, particularly albumin. Serum AG falls by 2.3 to 2.5 meq/L for every 1 g/dL (10 g/L) reduction in serum albumin concentration. If the normal serum albumin is considered as 4 gm/dl and the patient's albumin is 2 gm/dl, an observed AG of 12 should be interpreted as17 meq/L.

Anion gap can be rewritten as (unmeasured anions – cations), since

measured + unmeasured cation = measured + unmeasured anions.

Hence alterations in the unmeasured cations and anions can change the anion gap even in the absence of overt acidosis.

Normal Anion Gap Metabolic Acidosis (NAGMA) is otherwise called hyperchloremic acidosis. Both type II renal tubular acidosis (proximal) and diarrhoea will be characterized by loss of bicarbonate through urine and gut respectively, and the loss of bicarbonate is replaced by equimolar amount of chloride (meq for meq). Some patients with renal failure also develop normal anion gap metabolic acidosis.

Table 1. Causes of NAGMA

No.	Type	Specific causes
1	Loss of bicarbonate/ bicarbonate precursors	Diarrhoea or other intestinal losses (eg. tube drainage) Type 2 (proximal) RTA Post-treatment of ketoacidosis Carbonic anhydrase inhibitors Ureteral diversion (eg. ileal loop)
2	Failure of H^+ ion excretion	Type 1 (distal) RTA Type 4 RTA (hypo-aldosteronism)

*MNEMONIC for **NAGMA - USED CARP** (**U**reteroenterostomy, **S**aline hydration, **E**ndocrinopathies (hyperparathyroid, hyperthyroid, Addison's), **D**iarrhoea/ DKA/ Drugs, **C**arbonic anhydrase inhibitors, **A**mmonium chloride, **R**enal tubular acidosis, **P**arenteral nutrition/ pancreatic fistula).*

Metabolism of dietary proteins leads to generation of 50-100 meq of H^+ ions mainly in the form of sulphuric acid (H_2SO_4). When there is a significant tubular dysfunction there is a failure of excretion of H^+ ions and a failure of reabsorption of SO_4 ions. This results in the retention of chloride ions, thereby resulting in hyperchloremic acidosis. In patients with renal tubular acidosis type I and type IV there is retention of H^+ ions which is buffered by bicarbonate, with consequent reduction in bicarbonate. The bicarbonate loss is compensated by retention of chloride (delta bicarbonate = delta chloride).

High Anion Gap Metabolic Acidosis (HAGMA) occurs when there is accumulation of H^+ ion with a corresponding pathological anion, eg., accumulation of lactic acid, keto acid, oxalic acid, etc.

$$HL + NaHCO_3 \rightarrow NaL + H_2CO_3 \rightarrow H_2O + Co_2$$

In this reaction one molecule of HL i.e., lactic acid is buffered by one molecule of bicarbonate, generating one molecule of carbonic acid. If we assume that normal bicarbonate is 24 meq/L and 10 m mol of lactic acid has been retained, this 10 m mol of lactic acid will be buffered by 10 mmol of HCO_3, and the result will be generation of 10 mmol of H_2CO_3 and 10 mmol of sodium lactate. Also the bicarbonate will be reduced by 10 mmol/L. The new level of bicarbonate will be 14 meq/L. Due to the addition of the new lactate of 10 m mol/L, the anion gap increases by 10 mmol. In other words delta bicarbonate = delta anion gap, which is a cardinal feature of HAGMA.

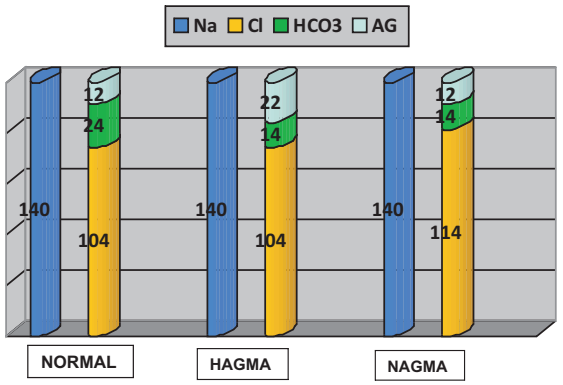
Table 2. Causes of HAGMA due to increased acid production

No.	Cause
1	Lactic acidosis
2	Ketoacidosis
3	Diabetes mellitus
4	Starvation
5	Alcohol associated
6	Ingestions Methanol Ethylene glycol Aspirin Toluene (if early) Pyroglutamic acid (5-oxypraline)

*MNEMONIC for **HAGMA – MUDPILES** (**M**ethanol, **U**remia, **D**KA, **P**araldehyde, poisoning, **I**NH, iron, **L**actic acid, **E**thanol, ethylene glycol, **S**alicylates)*

Aetiology of HAGMA:-

1. Lactic acidosis - type A and type B
2. Keto acidosis - diabetes mellitus, starvation, alcoholism
3. Uraemia
4. Poisoning - ethylene glycol (the metabolic product of oxalic acid), methyl alcohol (metabolic product of formic acid)
5. The anion gap is modestly elevated in hyperosmolar non-ketotic state (even though there is no acidosis), due to release of unmeasured anions such as phosphates.
6. In most cases of renal failure there is accumulation of H^+ ion and pathological anions such as phosphate, sulfate, urate, etc.



NORMAL AG: **Na – (Cl+HCO_3)** = 140 – (104+24) = 12

HAGMA: 140 – (104+14) = 22 [delta HCO_3 = delta AG]

NAGMA : 140 – (114+14) = 12 [delta HCO_3 = delta chloride]

Table 3. Major plasma anions & cations, and AG (normal & metabolic acidosis)

Overlap of HAGMA and NAGMA

1. Diarrhoea is typically associated with NAGMA due to loss of bicarbonate. In severe diarrhoea as in cholera AG can be increased due to a triad of hypoperfusion induced lactic acidosis, hyperalbuminemia due to volume contraction, and hyperphosphatemia due to shift from intracellular compartment due to acidosis.
2. Diabetic ketoacidosis typically produces HAGMA. If renal function is well preserved with good perfusion ketone bodies are eliminated as their Na or K salts, and results in loss of potential bicarbonate. The rise in AG will be less than anticipated.
3. Similar situation prevails in D-lactic acidosis and toluene induced metabolic acidosis. AG may be elevated or normal (if elimination of D-lactate and hippurate anions occurs with preserved renal function).

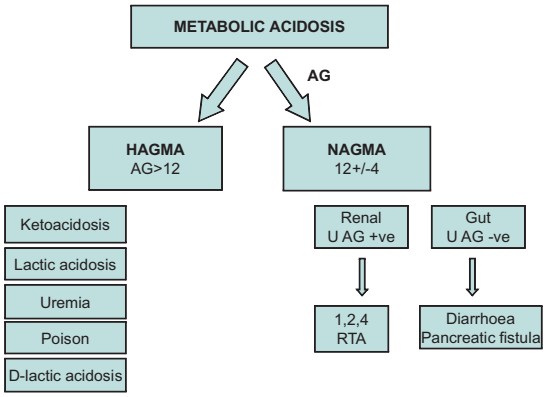


Fig. 1: Causes and aetiology of metabolic acidosis

Anion gap alterations in conditions other than metabolic acidosis

Anion gap can be low or high in other conditions as well. Hence anion gap in the patients should be interpreted in the light of other confounding factors.

An equation for Anion gap is:

unmeasured anion – unmeasured cations.

Anything that alters the unmeasured cations or anions can naturally alter anion gap. The most common cause for low anion gap is lab error.

Low anion gap can occur due to either decrease in the unmeasured anion or increase in the unmeasured cation. In the former category the most important cause is hypoalbuminemia. The serum AG falls by 2.5 meq/L for every 1 gm/dl reduction in the albumin concentration. In the latter category low anion gap arises from hyperkalaemia, hypercalcaemia, hypermagnesemia, lithium intoxication and multiple myeloma with paraproteins existing as unmeasured cations. This occurs when the paraproteins have an isoelectric pH of 9.4 and they exist as cations in the normal pH of 7.4. IgG myeloma is more likely to produce this phenomenon. Polyclonal IgG gammopathy has also been reported to present with a reduced anion gap.Anion gap can be rendered negative due to laboratory artifact of measurement of sodium or chloride. In severe hypernatraemia with serum Na above 170meq/L, Na gets under-estimated. Measured anion viz. chloride gets overestimated in the following situations:

a) Extreme degree of hyperlipidaemia produces overestimation of chloride due to the light scattering effect when colourimetric assay is used

b) Salicylate can be detected as chloride by chloride electrodec) Bromide intoxication (pyridostigmine bromide in herbal medications): each meq of bromide is measured as 2-3 meq of chloride.

GAPS in Metabolic acidosis:

1) Anion gap in serum

2) Osmolar gap in plasma

3) Urinary anion gap

1. The significance of the anion gap in plasma has already been discussed.
2. Osmolar gap in plasma has important implications. It refers to the difference between the measured osmolality and calculated osmolality. Measured osmolality is obtained by direct measurement and is the true osmolality.

The calculated osmolality is obtained using the formula viz.,

Na x 2 + (urea in mg/dl) ÷ 6 + (glucose in mg/dl ÷18).

The difference between measured osmolality and calculated osmolality is normally less than 10-15 mosmol/kg. If the difference is more than 15 mosm/kg, 'osmolar gap' is said to exist.

If a patient has HAGMA + osmolar gap the patient is said to have 'double gap acidosis' (eg. ethylene glycol poisoning, methanol poisoning).

3. Urinary anion gap is also useful in identifying the cause of NAGMA.

UAG = (UNa + UK) - UCl

Normally it is positive as Na and K together exceeds chloride. In cases of NAGMA, due to the loss of HCO_3 through gut, the following situation prevails. Acidosis being a stimulator of NH_3 production and kidney being normal, it secretes maximum NH_3 and excretes it as ammonium chloride for electrical neutrality. Thus there is increased unmeasured cation in urine. The chloride exceeds (Na + K) and the UAG {(UNa+K)-UCl} becomes negative. A negative UAG favours the diagnosis of NAGMA due to bicarbonate loss through the gut.

In RTA, NH_3 production is impaired and hence (Na + K) remains greater than chloride, and hence UAG remains positive as in the normal situation.

Few salient points regarding metabolic acidosis:

- *Ketoacidosis:* It may be due to DKA, starvation or alcoholism. In ketoacidosis the ketone bodies may not be detectable by conventional nitroprusside test when the patient is in shock. Shock is characterized by NADH/NAD system working in a more reduced state. In this situation NADH will convert the acetoacetic acid into beta hydroxy butyric acid, which cannot be identified by either Rothera's test or Gerhardt test. In shock state with severe ketoacidosis, ketone body can be negative by conventional methods, and a negative test does not eliminate ketoacidosis. Similarly in alcoholic ketoacidosis beta hydroxy butyric acid predominates and tests for ketone bodies can be negative despite severe ketoacidosis.

- *Poisoning due to Ethylene glycol* can be identified by *Double Gap acidosis* (anion gap and osmolar gap) and presence of envelope shaped oxalate crystals. Methanol also produces double gap acidosis, and the patient's vision is threatened with retinal oedema or papilloedema and blindness.

- *Aspirin poisoning* is characterized by triple abnormalities in ABG, i.e., HAGMA due to acetyl salicylic acid itself and lactic acidosis due to uncoupling of oxidative phosphorylation in mitochondria, respiratory alkalosis due to direct stimulation of respiratory centre, and metabolic alkalosis due to persistent vomiting.

- *Type I RTA* is distal hypokalemic type. There is failure of acidification by the distal tubule, and urinary pH is always above 5.5, despite acidosis. Urinary anion gap is positive. There is a tendency for stone formation/ nephrocalinosis. Important causes include auto immune disorders especially Sjogren's disease, rheumatoid arthritis and hyperglobulinemia. The RTA *Type I* patient has to be screened for Sjogren's syndrome. Drugs like cyclophosphamide and ifosamide can also be responsible for the condition.

- *Type II RTA* is characterized by reduced plasma bicarbonate reclamation from proximal convoluted tubule, so that there is urinary loss of bicarbonate. Occasionally the defect can be isolated. Often it is part of Fanconi's syndrome (generalised tubular dysfunction, glycosuria, phosphaturia, aminoaciduria, uricosuria, tubular proteinuria). The most common cause is multiple myeloma in the adult. There is increased fractional excretion of bicarbonate, when bicarbonate loading is done.

- *Type IV RTA* is due to aldosterone deficiency or tubular resistance to aldosterone: The most common cause is hyporeninemic hypoaldosteronism due to mild to moderate renal failure, especially in diabetes mellitus. Other causes include congenital adrenal hyperplasia, Addison's disease, tubulo-interstitial diseases and potassium sparing diuretics. Urine pH is less than 5.5, and serum potassium is high. This is the hyperkalemic variety of distal RTA.

Conclusions

The approach to metabolic acidosis will include:

1. Establish that there is metabolic acidosis using ABG analysis
2. Find out whether it is HAGMA/ NAGMA
3. Know four causes of HAGMA (ketoacidosis, lacticacidosis, renal failure & toxins)
4. Know two causes of hyperchloremic or nongap acidosis (HCO_3 loss from GI tract & renal tubular acidosis)
5. Include osmolar gap for analysis of HAGMA
6. In NAGMA include UAG to identify the status of NH_3 secretion and source of HCO_3 loss, and identify whether the gut or the kidney is at fault

Treatment of the disorder has to address the cause.

✪ TECHNICAL REPORT

Part III - Towards a scientific basis for health systems

"Health systems should nurture a stronger culture of learning and problem-solving to tackle the major health challenges of our times"
(Tim Evans)

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The health systems in the developing world face major problems related to shortages, maldistribution and waste of the financial, human, knowledge and other resources, and coverage shortfalls (Table 3.1). There is increasing recognition by major health initiatives that many of their efforts to improve health share the same common health system constraints. Despite acknowledgement of its importance and potential to overcome health system constraints, health systems research suffers from a poor image and has been neglected and under-funded compared to other areas of health research. Key research issues and knowledge gaps pertaining to human resources, financing, health information and delivery of health services must be addressed in the context of more emphasis on broader health systems strengthening. Based on a readiness to reach beyond the traditional academic disciplines, new innovations, latest methodologies and better tools should be developed for health systems research. A substantial programme for supporting the development of a new paradigm for research to strengthen health systems is required in the near term if health systems are to perform more effectively and improve health outcomes.

Some Interesting numbers are given below:

- Two percentage of global health expenditure is in Africa, which carries 25% of the global burden of diseases. In contrast, 90% of global health spending is in the developed countries with 20% of the world's population.
- Two percentage of countries in WHO's South-East Asia regions that have complete coverage of death registration data, as opposed to 75% in the European region.
- 0.71 percentage of papers are on the subject of health systems and health services research in the year 2000, based on a search of Medline.
- 0.1 percentage of total funds are allocated to health systems research, as a portion of total health expenditure in developing countries.

Bottlenecks and constraints in health systems

The major constraints and challenges currently facing health systems in the developing world include: workforce shortages, limited financing, scant or poor quality health information, problems with quality, and inability to scale up rapidly. Despite the importance given to health achievement, there is a growing body of evidence pointing to a shortage of about four million health workers globally. Recent evidence (Fig. 3.1) suggests that more health workers can be associated with lower infant, child and maternal mortality.

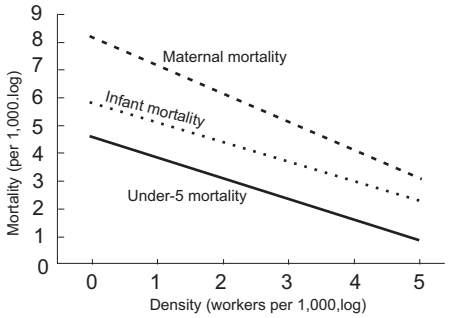

Fig. 3.1 Relationship between mortality rates and health workforce

* Adapted from WHO report on **Knowledge for Better Health, Geneva 2004**

Continued from page 115, PMJ Vol 1, No.2

The countries in the Organization for Economic Development and Cooperation (OECD), which represents much of the industrialized and developed world, are facing shortages of health workers too, mainly due to an expansion of the health sector. These shortfalls are being met increasingly by workers from poorer countries. In countries where health workers are already scarce, increasing migration is associated with the interruption of life-saving services sometimes referred to as "fatal flows" in the health workforce. The migration of health workers also occurs within countries where nurses and doctors are lured away from the public sector by higher private sector pay, and the magnet of urban life depletes the workforce in rural areas.

Beyond these shortages, there are a number of factors that prevent health workers from having the best opportunities to improve health and alleviate suffering. Antiquated curricula in medical schools mean that professionals are often ill-equipped to respond to the needs of the population, creating a so-called *"skills-gap"*. The primary employers of health workers including governments, NGOs and the private sector often fail to provide "productive" working conditions. These range from irregular to inadequate pay, an absence of requisite supplies such as drugs and diagnostics, as well as a lack of incentives to encourage workers to serve in remote, isolated locations (Fig. 3.2)

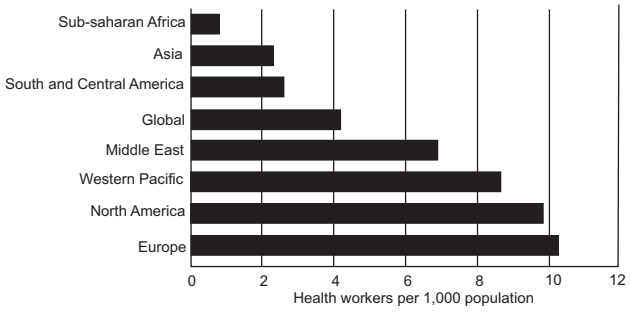

Fig. 3.2 Global health workforce by region

Financing

Not only a massive mobilization of human resources, but also a substantial financial resourcing is needed for the health sector in a number of countries. So also, unfortunately, people in many countries have access to health care but only at great personal expense and, in many cases, they may be pushed into poverty. High levels of what is known as out-of-pocket payment leads to financial catastrophe and impoverishment for many households.

To help countries meet these challenges, it is important to find ways to routinely obtain information on key financing parameters. This includes information on how much is spent, by whom and for what, and whether households suffer catastrophic financial payments. It also includes information on the costs, effectiveness and implications for equity of using health resources in particular ways, something that is necessary to decide how best to achieve stated health system objectives.

Health information

On his first day of office in an address to staff of WHO, the former Director-General, Dr Lee Jong-wook, described health information as the *"glue that holds health systems together".* In the remarks on the need to strengthen and integrate health information systems at country level, he noted that countries with the highest disease burden are the least likely to count births and deaths, and he concluded that *"to make people count, we first need to be able to count people".* The *"gold standard"* of national registration systems currently covers only one third of estimated global mortality. Many countries cannot even count their dead (Table 3.2).

Table 3.1 Availability of death Registration data in WHO regions

Region	*Usable data*	*Complete coverage*	*Total countries*
Africa	4	1	46
Americas	32	14	35
South-East Asia	4	0	11
Europe	48	39	51
Eastern Mediterranean	7	4	22
Western Pacific	22	8	27
Total	**117**	**66**	**192**

The aim of the health information system is to collect, process, report and use the health information and knowledge to influence policy-making, programme, action and research. In practice, health information systems lack cohesion, having developed in a piecemeal way, fashioned by administrative, economic, legal or donor pressures. Responsibility for health information is sometimes spread across different ministries or institutions within a country. Ministries and institutions often resist co-ordinating this due to financial and administrative constraints. Special efforts are needed to ensure that the distribution of this information is co-ordinated properly and shared with the health sector.

Health services delivery

The human, financial, information, and technical/ material resources of a health system merge to provide effective health services. At present, this "merging" or in other words co-ordinating these "health services" fall far short of the performance expectations of important health outcomes. Not only are the populations in the greatest need not receiving tried and tested treatment and medicines, but many health problems remain invisible as well. People who turn to the system for health care, sometimes at great personal expense, often fail to receive intended health benefits. This disappointing performance of the health system is

of great concern and requires a more fundamental understanding of its complex determinants.

Ensuring equitable, universal access to health care, whether preventive, promotive or curative, is a key objective of health systems. Key constraints in achieving this relate to low levels of coverage for many priority interventions, poor co-ordination and weak infrastructure. Conflicting agendas of donor programmes and diversion of trained workers into high-profile initiatives compound the problem in developing countries.

Health systems research

Given the enormous challenges facing health systems today, a robust and sound research enterprise is critical in generating the knowledge needed to overcome these constraints. This area of research is referred to as health systems research.

What is health systems research?

Health systems research is defined as the generation and utilization of new knowledge to improve the way societies achieve their health goals. This may include the way they plan, manage and finance efforts to improve health, as well as involving and engaging all interested sectors of society. Health systems research is essentially research that investigates strategies for improving health service delivery, including the use of sound evidence in developing such strategies and in shaping effective health policy. It may be applied both within institutions, communities and at district or at national level.

Health systems research has not always been successful in attracting the best minds, and seems unable to compete with scientific disciplines such as biomedical and clinical research which are seen as more glamorous and high-profile. Similarly, career prospects and advancement within academia seemed more limited for those choosing this career path. In large organizations dealing with health, such as ministries of health and WHO, administrative structures are often not conducive for allowing health systems research to flourish. Table 3.3 lists some of the possible reasons for this relative neglect.

Table 3.3 Reasons for neglect of health systems research

- *Health systems have an image problem:* visible or emotive topics such as child deaths or polio campaigns engage stakeholders in ways that interventions for strengthening planning or account-ability mechanisms do not.
- *Health systems research also has an image problem:* other forms of research such as basic sci-ence and drug discovery are prestigious while health systems research is seen as fluffy, pedestrian and applied.
- *Divergent views on the types of questions amenable to scientific enquiry:* some believe that health system problems are primarily political, and therefore best solved using common sense rather than evidence.
- *Answers from such research can be slow to arrive and uncertain,* because of the long-term nature of health systems change
- *Generalization can be difficult,* because the effects of interventions crucially depend on the envi-ronment in which they are implemented.
- *Health systems research may not have disease- or intervention-specific focus,* so there are fewer research opportunities for research funding.
- *Disinterest and difficulty in assessment:* because the interventions are part of large messy reforms with strong political imperatives; systematic evaluations are difficult to design and may be difficult to defend.
- *Restricted research capacity, and a research workforce that is multi-disciplinary* and therefore does not have an obvious institutional home with clear career structures.
- *The right questions are not being asked:* improved understanding is needed about the types of research that really changes the way decision-makers think.

A recent priority setting workshop in human resources for health (HRH) research proposed that research should be organized around seven themes:

1. Assessment, policy and planning
2. Managing size, skill mix and organization
3. Using incentives to improve performance
4. Mobility
5. Educating and training
6. Legislation and regulation
7. Influence of political and economic contexts on the developing national HSR strategies and policies

A call for action

Health systems research is in need of a new paradigm. The future cannot be business as usual. For health systems research to be elevated to the same status as molecular biology and genomics, substantial and sustainable resources and support must be mobilized. A “grand challenges” approach should be considered for health systems research, to develop interventions to deal with global health challenges.

However, it is not just about more funding. It requires a concomitant commitment and passion from the health research community itself, and a willingness to think creatively and be more open to new ideas. Unless this happens, health systems research may be unable to escape the den of scientific poverty and inequity.

(Concluded)

✪ CME REPORT

OTOENDOCON - 2010

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Endoscopic sinus surgery has revolutionized the treatment of sinus pathology over the past few years. It has developed as a specialty within ENT. More so, the specialty has started expanding beyond the limits of the nasal cavity into the orbit and anterior skull base. The department of ENT, Pushpagiri Medical College and Association of Otolaryngologists of India (AOI) Central Travancore Chapter jointly organized OTOENDOCON 2010, an International Workshop on Endoscopic Sinus Surgery and temporal bone dissection.

Following the success of our first endoscopic hands on workshop last year, we decided to take a stride further this year, by incorporating temporal bone dissection course as well. Around 30 delegates were provided an opportunity to fine-tune their skills in cadaveric temporal bone dissection and endoscopic sinus surgery. The workshop was led by eminent faculty of international fame, such as Prof. Reda Kamel, Prof of Rhinology, University of Cairo, Dr. Nishit Shah, Endoscopic Skull Base Surgeon from Mumbai, Dr. Janakiram, ENT surgeon from Trichy and Dr.Viyayendra, Otologist from Bangalore.

Live demonstration of Endoscopic Sinus Surgery with state-of-the-art equipments was a highlight of the three day workshop. As many as 70 practicing ENT surgeons from all over India and the Middle East participated in the workshop. We intend to have such workshops on a yearly basis so as to provide a platform for budding ENT surgeons in the Kerala state, and the country at large.

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✪ BOOK REVIEW

Clinical Surgery Pearls

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"Clinical Surgery Pearls" is an excellent book, which will be of immense use to medical students, teachers and practicing surgeons alike. The author's systematic approach to the surgical problems, with special focus on the Indian perspective of diseases, has to be well appreciated. Arrangement of the various sections as definitions, case discussions, radiographs and charts is quite useful. The subject matter is arranged in points, and uses flow charts, algorithms and box information, which can be easily remembered.

The book provides a practical, step by step guide to learning General Surgery. In all the case discussions the author stresses on the basics of diseases and the various changes taking place in the Anatomy and Physiology of the organ systems, which form the basis for clinical examination. It is liberally illustrated, with the text presented in simple and clear language. The presentation is simple and self explanatory and can be followed easily by an average student. It is very useful for a rapid revision just prior to the University examination at UG and PG level.

The entire General Surgery has been covered systematically, with the imaging and standard surgical procedures added. The book is compact to the pocket size of the overcoat. The index, print and paper quality looks excellent.

I sincerely appreciate the magnitude of effort taken by, and the unfailing enthusiasm and perseverance of the author in bringing out this book in this excellent manner, and hope it will be a real 'pearl' for all medical students in Surgery. I strongly recommend this book for undergraduates, postgraduates and teachers of the Department of General Surgery.

PUSHPAGIRI MANUAL FOR HOUSE SURGEONS

House surgeoncy is the period during which the grooming doctors begin to practice clinically what they have studied theoretically in their undergraduate curriculum. This great venture of preparing a manual by Dr R Dayananda Babu provides guidelines to the principles of bedside management of common clinical problems confronted by house surgeons during their resident period. The manual begins citing the model code of conduct, and outlines the duties and responsibilities of house surgeons. The highlight of this manual is that the procedures, techniques, and management of emergency conditions in different clinical departments are handled by experts in the corresponding field themselves, including the super-specialists. This will help the fresh medical graduates to learn the techniques in a precise manner.

Dr R Dayananda Babu deserves appreciation and credit for visualizing a project of this magnitude, involving all clinical departments, and materializing the same. All the matter in the manual have been compiled and presented in a simplified and at the same time, systematic manner. This will prove a boon to all house surgeons in their day to day work.

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