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Ahmad Husari

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In this issue a number of papers came from Jordan dealing with various aspects of health. A Retrospective study of patients diagnosed to have obstructive sleep apnea syndrome between 2013 and 2015. Epworth Sleepiness Scale score and Apnea-Hypopnea Index of 118 patients were compared. Of the 118 patients diagnosed to have Obstructive Sleep Apnea Syndrome, 65 patients had a score of >10 on the Epworth Sleepiness Scale, which translates to 55% of the patients studied. 100% of patients with severe OSAS had an ESS score >10. However, in patients with moderate and mild OSAS, 46.5% and 36% scored >10 on the ESS respectively. The authors concluded that Epworth Sleepiness Scale is sensitive in patients with severe OSAS. However, the accuracy of the ESS becomes less in mild and moderate OSAS, making it a poor and non-accurate screening method for OSAS.

A paper from Jordan assessed the pregnancy course and perinatal bleeding in women with severe autoimmune thrombocytopenic purpura. Data was collected for 38 pregnancies in 24 women, who were on treatment for autoimmune thrombocytopenic purpura early in pregnancy. Indication for treatment was platelets count 50,000/mm3 or less. We looked for premature rupture of membranes, premature delivery, intrauterine growth restriction and significant blood loss at delivery. Those women were the study group, (group 1). Same variables were looked for in 100 healthy pregnancies taken as control (group 2). Data was compared between the two groups. Women who had thrombocytopenia secondary to other conditions such as, systemic lupus, bone marrow diseases and other causes were not included in the study. The results showed that study group 1 had nine premature rupture of membranes in 38 pregnancies, whereas only ten women ruptured their membranes out of 100 in control group 2 with an odds ratio 2.9. Four women had significant blood loss at delivery in group 1 and eight women in group 2 which presents marginal increase for group 1 (odds ratio 1.3). No increase in growth restricted babies nor in premature delivery was noticed. The authors concluded that pregnant women with autoimmune thrombocytopenic purpura on treatment, have significant higher risk to rupture their membranes prematurely. No increase in growth restricted babies and premature deliveries. With good care they can deliver safely with minimum hazard of bleeding.

A paper from the ENT department studied 54 patients ages between 12 & 46 years ,with mean age of 21.3 years, who proved to have ACP investigated by CT-Scan during 3 years period (between may 2009 & feb..2012 ) were retrospectively evaluated and follow up imaging CT-Scan was performed for this group of patients. The aim of this study was to evaluate the common radiological features in initial and post operative follow up imaging of patients proved to have antrochoanal polyp, and who were treated surgically ,and to evaluate post operative clinical improvement of this sample. Unilateral polyposis was found in 38 patients ( 70.4%) and bilateral in 16 patients ( 29.6%). All patients were operated by Functional Endoscopic Sinus Surgery (FESS).The patients were followed up by CT-Scan axial and coronal views at 4-6 weeks post operatively and only in 7 patients we recorded a post operative inflammatory findings of which in 2 patients the diagnosis was recurrent antrochoanal polyp. The authors concluded that CT-Scan was very accurate in diagnosing antrochoanal polyp in pre and post operative assessment and the recurrence of this disease was very minimal according to follow up clinical and imaging results.The Functional Endoscopic Sinus Surgery (FESS) was very effective in preservation of normal antral mucosa with minimal complications in post operative follow up.
Evaluation of Epworth Sleepiness Scale as a screening method for Obstructive Sleep Apnea Syndrome (OSAS)

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ABSTRACT

Objective: To compare the results of the Epworth Sleepiness Scale (ESS) score and the Apnea-Hypopnea Index (AHI) measured by overnight polysomnography in patients diagnosed to have Obstructive Sleep Apnoea Syndrome in King Hussein Medical Center (KHMC), to evaluate the Epworth Sleepiness Scale as a screening method for OSAS.

Method: Retrospective study of patients diagnosed to have obstructive sleep apnea syndrome between 2013 and 2015. Epworth Sleepiness Scale score and Apnea-Hypopnea Index of 118 patients were compared.

Results: Of the 118 patients diagnosed to have Obstructive Sleep Apnea Syndrome, 65 patients had a score of >10 on the Epworth Sleepiness Scale, which translates to 55% of the patients studied. 100% of patients with severe OSAS had an ESS score >10. However, in patients with moderate and mild OSAS, 46.5% and 36% scored >10 on the ESS respectively.

Conclusion: Epworth Sleepiness Scale is sensitive in patients with severe OSAS. However, the accuracy of the ESS becomes less in mild and moderate OSAS, making it a poor and non-accurate screening method for OSAS.

Key words: Epworth Sleepiness Scale (ESS), Obstructive Sleep Apnoea Syndrome (OSAS), screening
Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is common, affecting approximately 4% of middle-aged men and 2% of middle-aged women. (1) However, these figures are an underestimate, and about 95% of patients with sleep disorders are not diagnosed. (2,3) It is very important to diagnose and manage OSAS efficiently, because OSAS is independently associated with increased morbidity and mortality due to cardiovascular and neurovascular diseases, metabolic disorders and impaired neurocognitive function. (4,5,6)

Overnight polysomnography (PSG) is the gold standard for diagnosing OSAS. However, the PSG is expensive, time consuming and not widely available outside big medical centers. Another problem is the long waiting time for PSG. All of these issues urge us to find a simple and reliable way to screen patients for the probability of OSAS before referring them to an overnight polysomnography.

Many tests have been evaluated and studied. The Multiple Sleep Latency Test (MSLT) is believed to provide a reliable measurement of sleepiness. (7,8) The Maintenance of Wakefulness Test (MWT) (9) and the Modified Assessment of Sleepiness Test (MAST) (10) were also shown to be reliable when it comes to evaluating patients with sleep disturbances. However, all these tests have the same disadvantage of being cumbersome, expensive and time consuming.

The Epworth Sleepiness Scale was developed in 1991, and was suggested as a screening method for patients with suspected OSAS. Despite the fact that it is subjective, ESS has the advantage of being fast, free and easy to be applied. (11)

Our aim in this study is to evaluate the Epworth Sleepiness Scale (ESS) as a screening method for OSAS.

Methods

The study was done by analyzing the files of 118 patients who underwent overnight polysomnography (PSG) in KHMC between 2013-2015. They were all diagnosed to have OSAS (defined as AHI>5). The pre-treatment ESS score of these patients was compared to their Apnea-Hypopnea Index (AHI) obtained during the PSG. An ESS score of >10/24 is considered to be suggestive of excessive daytime sleepiness (EDS) (12), and warrants further evaluation by PSG to rule out OSAS.

Results

In our study group which consisted of 118 patients with OSAS, 47 patients had mild OSAS (defined as AHI 5-15), 43 patients had moderate OSAS (AHI >15-30) and 28 patients had severe OSAS (AHI>30).

By comparing the results of the ESS score and AHI of these patients, it was found that 65 patients from our study group had an ESS score >10. This represents 55% of the patients included in the study.

All 28 patients with severe OSAS had an ESS score>10, which means that ESS score was suggestive of EDS in 100% of patients with severe OSAS in our study group.

From the 43 patients diagnosed with moderate OSAS, 20 patients had an ESS score>10, which means that 46.5% of patients with moderate OSAS in our study group had an ESS score suggestive of EDS.

From the 47 patients with mild OSAS, 17 patients had an ESS score>10. This means that 36% of patients with mild OSAS in our study group had an ESS score suggestive of EDS.

Table 1: The number and percentage of patients with ESS>10 in the mild, moderate and severe OSAS groups

<table>
<thead>
<tr>
<th>OSAS (AHI)</th>
<th>MILD (5-15)</th>
<th>MODERATE (16-30)</th>
<th>SEVERE (&gt;30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>47</td>
<td>43</td>
<td>28</td>
</tr>
<tr>
<td>Number of patients with ESS&gt;10</td>
<td>17</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>% of patients with ESS&gt;10</td>
<td>36%</td>
<td>46.5%</td>
<td>100%</td>
</tr>
<tr>
<td>Total % of patients with ESS&gt;10</td>
<td>55%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Epworth Sleepiness Scale (ESS) was developed in 1991 by Dr. John W. Murray. It consists of 8 questions that are supposed to evaluate the tendency of an individual to fall asleep in certain conditions. Each question is answered by a number on a scale from 0 to 3 (Chart 2 - opposite page.)
Chart 1: Comparison between total number of patients diagnosed to have OSAS (mild, moderate and severe) and the number of those with ESS>10

Chart 2: Epworth Sleepiness Scale form

0 = No chance of dozing off    2 = Moderate chance of dozing off
1 = Slight chance of dozing off   3 = High chance of dozing off

Rate the chance that you will doze off in the following situations:
- Sitting and reading
- Watching television
- Sitting inactive in a public place (e.g. in a theatre, during a meeting)
- As a passenger in a car riding for an hour without break
- Lying down to rest in the afternoon when circumstances permit
- Sitting and talking to someone
- Sitting quietly after lunch without alcohol
- In a car while stopped for a few minutes in traffic

Add above total score
After answering all the questions in the ESS form, a score of >10 is considered to be suggestive of excessive daytime sleepiness (EDS), and OSAS is highly suspected in this group of patients, which warrants further evaluation by overnight polysomnography. However, and according to Dr. Murray, the evaluation by the ESS is influenced by the patient’s reading and comprehension skills and honest answers. (11)

In our study, it was shown that the ESS is very sensitive in patients with severe OSAS. All 28 patients with AHI>30 had an ESS score>10, with 100% sensitivity of ESS in detecting EDS in this group.

However, the sensitivity of the ESS gets less when it comes to patients with mild and moderate OSAS.

From the 47 patients diagnosed to have mild OSAS in our study, 17 patients had an ESS score >10, which means that only 36% of these patients had an ESS score suggestive of EDS.

In the group of patients with moderate OSAS which consisted of 43 patients, 20 patients had an ESS score >10, which means that 46.5% of them had an ESS score suggestive of EDS.

Overall, 55% of the patients who were diagnosed to have OSAS in this study had an ESS>10, leaving nearly half of the patients (45%) with an ESS score NOT suggestive of EDS. This means that the ESS has a low sensitivity as a screening method for OSAS.

This result was also concluded by other studies, such as the meta-analysis done by Ramachandran and Josephs (13), which evaluated several clinical screening tests for OSAS. They concluded that the ESS was the least accurate of all the screening tests examined in the study.

Conclusion

The ESS is a very simple, cheap and fast way to assess patients for the possibility of EDS and OSAS. However, it has low accuracy in the mild and moderate OSAS groups.

Patients with mild and moderate OSAS are still at high risk for cardiovascular and neurovascular diseases and metabolic abnormalities, and failure to detect these patients through screening methods will delay their diagnosis, and thus will delay offering them good management of their OSAS, putting them at higher risk for complications of these diseases. This makes the Epworth Sleepiness Scale (ESS) not a preferable method for screening for OSAS, and it can’t be used as a sole screening method for OSAS.

References

Imaging of antrochoanal polyposis

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ABSTRACT

Objective: The aim of this study was to evaluate the common radiological features in initial and post operative follow up imaging of patients proved to have antrochoanal polyposis, and who were treated surgically, and to evaluate post operative clinical improvement of this sample.

Methods: A total number of 54 patients ages between 12 and 46 years, with mean age of 21.3 years, who proved to have ACP investigated by CT-Scan during a 3 year period (between May 2009 and February 2012) were retrospectively evaluated and follow up imaging CT-Scan was performed for this group of patients. The main presenting clinical symptom of the selected patients was nasal obstruction. We selected a coronal sinus CT-Scan as referral imaging modality for this study and according to which we made our calculations and conclusions.

Results: Unilateral polyposis was found in 38 patients (70.4%) and bilateral in 16 patients (29.6%). All patients were operated on by Functional Endoscopic Sinus Surgery (FESS). The patients were followed up by CT-Scan axial and coronal views at 4-6 weeks post operatively and only in 7 patients we recorded a post operative inflammatory finding of which in 2 patients the diagnosis was recurrent antrochoanal polyp.

Conclusion: We conclude that CT-Scan was very accurate in diagnosing antrochoanal polyp in pre and post operative assessment and the recurrence of this disease was very minimal according to follow up clinical and imaging results. The Functional Endoscopic Sinus Surgery (FESS) was very effective in preservation of normal antral mucosa with minimal complications in post operative follow up.

Key words: Antrochoanal polyposis, CAT-Scan, FESS
Introduction

Antrochoanal polyposis (ACP) is not uncommonly found in the general population investigated for paranasal sinus pathology; it represents a herniated maxillary sinus polyp through the ostium reaching the nasopharynx in the majority of cases and accounts for about 3-6% of all paranasal polyps. Imaging of these patients plays an essential part in managing and follow up of surgical treatments. The prevalence of this pathology is more prominent in pediatric and young adult age groups.

Killian was the first to describe choanal polyp (CP) in 1906 and considered it as a large solitary polyp originating from maxillary sinus mucosa and redirected posteriorly reaching the nasopharynx. This process takes part through the accessory ostium of the maxillary sinus (1). Many recent studies prove that not only is the accessory ostium the solitary anatomical origin of this medical entity, but it can also originate from sphenoid sinus and sphenoidomidal recess and rare cases have been reported from the frontal sinus. This clarification was approached by the newly developed imaging modality machines, such as helical computerized tomography machines CAT-Scan and MRI. These pear shaped form antrochoanal polyps are seen usually solitary and unilateral in the majority of cases, differentiating them microscopically from common nasal cystic polyps (2).

The presenting features are common in children and young adult age groups (3). ACP recurrence after surgical removal is not uncommon in many studies being reported in literature (4). These lesions are usually benign and cause no bony or cartilaginous destructive changes of the maxillary boundaries, but can enlarge and extend in all directions. The commonest is the nasopharynx causing postnasal air route obliteration (5). Nowadays appropriate diagnosis is made by nasal endoscopy and computed tomography in axial and coronal views so as to make a final management plan for each case, considering that definite treatment is surgical in all cases (6). With improving new modalities of imaging machines, such as helical CAT Scans in multiplanar reformats, the diagnosis of these lesions is becoming more accurate excluding bony and dental artifacts (7).

Material and Methods

A total number of fifty-four patients, aged between 12 and 46 years, with mean age of 21.3 years, were retrospectively analyzed and investigated by CT-Scan (Mx 8000 Dual helical Philips) during a three year period (between May 2009 and February 2012). The main presenting clinical symptom of each patient was nasal obstruction. Axial and coronal CT-Scan in multiplanar reformat for the paranasal sinuses was performed for all these all patients and a follow up postoperatively according to clinical request was done. We selected coronal sinus CT-Scan as referral imaging modality for this study and according to which we made our calculations and conclusions.

Results

Among patients included in this study (Table 1), unilateral antrochoanal polyps were found in 38 patients (70.4%) and bilateral in 16 patients (29.6%). All patients were operated on by Functional Endoscopic Sinus Surgery (FESS). All patients were followed up 4-6 weeks post operatively and only in 7 patients we recorded a post operative inflammatory finding of which in two patients the diagnosis was recurrent antrochoanal polyp (Figure 3).

Discussion

Unilateral benign paranasal polyp represents a disease that affects the child age group as well as young adults with no preferences regarding the sex preponderance, and in a few recent studies male patients are slightly more frequently seen (8). The etiology of this disease is mentioned as uncertain, but many theories describe the previous inflammatory processes and allergy that affect the mucosal layers of the sinus as a predisposing factor which remain unproved for other groups of editors (9). Antrochoanal polyp usually arises from mucosal lining maxillary sinus in the majority of cases and extends posteriorly through an accessory ostium into the nasal cavity which can be enlarged to obliterate the choanal and nasopharynx. The patient is usually young adult who complains of unilateral nasal obstruction worsening on expiration. When the disease progresses, this can block the Eustachian tube. Many diagnostic modalities are implicated in supporting a management plan for ENT surgery physicians, nasal endoscopy, computerized tomography (CT-Scan) and magnetic resonance imaging (MRI) are considered the main investigations used to detect uni- or bilateral nasal polyposis. When CT-Scan is used, the diagnosis is made by detecting a mass which fills the maxillary antrum and which goes through the accessory or original ostium into the choana [Figure 1 & 2]. MRI shows T1 hypointense and T2 hyperintense lesions within the antrochoanal regions (10). In our study we used just CT-Scan as the diagnostic modality of choice for all patients; the axial and coronal reformats were the preferred methods of choice.

Table 1: Frequency of unilateral antrochoanal polyps and recurrence of post operative percentages

<table>
<thead>
<tr>
<th>Table 1: Frequency of unilateral antrochoanal polyps and recurrence of post operative percentages</th>
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<tbody>
<tr>
<td>Unilateral antrochoanal polyp</td>
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<tr>
<td>Bilateral antrochoanal polyp</td>
</tr>
<tr>
<td>Recurrence ACP</td>
</tr>
</tbody>
</table>
Figure 1: axial (a) & coronal (b) CT-Scan of 21 years old male patient showed huge lobulated right antrochoanal polyp filling right nasal cavity and post-nasal space.

Figure 2: Well defined soft tissue density polypoidal lesion arising from Right maxilla and extending posteriorly into nasopharynx of a 15 year old female patient. Note the complete blockage of Right Choana.
Differential diagnosis was made with other nasopharyngeal masses, including juvenile nasopharyngeal angiofibroma, meningoencephalocele, nasal glioma, hemangioma, adenoids and nasopharyngeal malignancy as well as lymphoma(11). A proper history and vigorous clinical evaluation along with careful selection of investigatory methods all were helpful in differentiating antrochoanal polyp from other suspected lesions. The frequent differential diagnosis was done with Juvenile nasopharyngeal angiofibroma due to similarity of presentations and almost affecting the same age groups of patients, which is usually highly vascular benign neoplasm with potential for local destruction, and it is commonly associated with epistaxis(12-14). Surgical removal was the method of choice in treating our patients and the Functional Endoscopic Sinus Surgery (FESS) was done for each patient. Complications were seen in a minority of patients which correlates well with other studies and did not exceed 4% of all cases, which is in the range of many international centers (15-17).

## Conclusion

We conclude that CT-Scan in axial and coronal views was sufficiently accurate in diagnosing antrochoanal polyp in pre and post operative assessment and the diagnostic nasal endoscopy remains in limited use. Recurrence of this disease was very minimal according to follow up clinical and imaging results. The Functional Endoscopic Sinus Surgery (FESS) was very effective in preservation of normal antral mucosa with minimal complications in post operative follow up screening.

## References


Subclinical Hypovitaminosis D and Osteoporosis in Breast Cancer Patients

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ABSTRACT

Objective: This study was designed to detect 25-hydroxy vitamin D serum levels and bone mineral density (BMD) status in breast cancer patients, and to determine their relation to treatment and disease stages.

Patients and methods: The study included 74 female patients with breast cancer and 52 healthy volunteers as the control group. Serum levels of 25-hydroxy vitamin D, calcium, phosphorus, and alkaline phosphatase were measured using ELISA kits, while dual energy x-ray absorptiometry (DXA) was performed to assess the BMD. Twelve patients received chemotherapy only; 12 received chemotherapy and hormonal therapy, 22 received chemotherapy and radiotherapy while 28 received chemotherapy, hormonal therapy and radiotherapy.

Results: Serum levels of phosphorus and 25-hydroxy vitamin D were significantly lower (p =0.0001), and alkaline phosphatase was significantly increased (p =0.0001) in patients compared to the control. Hip, spine, and forearm DXA were significantly lower in patients than in controls (p =0.0001). The worst bone status was in those receiving both chemotherapy and hormonal therapy. The grade of tumor significantly correlated with the serum phosphorus level (p =0.048) and negatively with the serum 25-hydroxy vitamin D level (p =0.03) as well as with the DXA of hip (p =0.01) and spine (p =0.0001).

Conclusion: Our study supports findings of increased incidence of hypovitaminosis D, osteoporosis and osteopenia in breast cancer patients. Hence, we throw light on the importance of offering calcium and vitamin D supplements to breast cancer patients. It is recommended that breast cancer patients have a DXA scan on a yearly basis.

Key words: Breast Cancer, DXA, 25-hydroxy vitamin D, bone mineral density.
Introduction

Among the long term problems associated with breast cancer is an increased incidence of bone loss and osteoporosis. This may be attributed to the disease itself or to the effect of chemotherapy, radiotherapy, and/or hormonal therapy [1,2]. Osteoporosis is a disease that affects bone structure and strength, leading to increased fracture risk [3]. Menopausal women experience a gradual decrease in bone density due to the effects of estrogen decline [4]. Many breast cancer patients experience a premature menopause that may be related to the effects of chemotherapy, direct radiotherapy, or surgical removal of the ovaries. There are specific chemotherapeutic agents (doxorubicin, cyclophosphamide, methotrexate, and 5-fluorouracil) that may play a major part in this process. In addition, hormonal treatment by aromatase inhibitors (AIs) such as anastrozole, letrozole, and exemestane play a pivotal role. Inhibition of the aromatase enzyme blocks the conversion of adrenal androgen into estrogen [5]. Using letrozole for 2 years had an impact on the bone mineral density (BMD), as the patients experienced a noticeable decline at the hip and lumbar spine, with more women becoming osteoporotic [6]. Corticosteroids that are commonly used in breast cancer metastases are known to cause bone loss. Moreover, breast cancer itself plays a role in this loss through activation of osteoclasts [7]. Vitamin D may help in prevention of breast cancer. While the association between vitamin D and breast cancer risk/prognosis is still controversial, a high proportion of women at-risk or affected by the disease have deficient vitamin D levels (<20 ng/ml) [8]. The best way to prevent bone loss associated with AIs is unclear, but it is advisable to practice exercises, receive calcium, vitamin D and bisphosphonate especially in post-menopausal women with a T-score less than -2.0 regardless of the fracture risk factors [9]. A guideline for the monitoring and treatment of bone loss associated with breast cancer has been published by the American society for clinical oncology (ASCO) [10].

Experimental studies have shown that 25(OH) vitamin D [11] calcium [12] and parathyroid hormone (PTH) [13] might affect tumor development. High levels of 1,25(OH) vitamin D in the breast might have an antitumor effect through the induction of cell differentiation, inhibition of cell growth and regulation of apoptosis in normal and malignant cells [14]. Vitamin D exerts its anti-tumor effect via its receptor to form a nuclear receptor-ligand complex which regulates the expression of target genes [15]. Not only does the active form of vitamin D inhibit breast cancer cells from growing, but it makes them grow and die more like normal cells. Moreover vitamin D has anti-angiogenesis effect [16].

The two naturally occurring vitamin D forms Ergocalciferol (vitamin D2) and colecalciferol (vitamin D3) can be obtained from natural foods, fortified products or supplements and D3 can also be synthesized from 7-dehydrocholesterol in skin exposed to ultraviolet radiation [17]. Following its synthesis in the skin or oral intake, vitamin D is converted to 25-hydroxy vitamin D in the liver. The 25(OH) D3 is the predominant circulating metabolite and correlates with vitamin D status [18]. Thereafter, 25(OH) D undergoes renal hydroxylation, tightly regulated by PTH and calcium concentrations [19]. Due to the widespread use of screening mammography and early detec-

tion programs leading to breast cancer diagnosis at a much earlier stage and the recent introduction of more effective anti-cancer therapy, more women are surviving their breast cancer, which highlights the need for survivorship programs that address issues like bone health [20].

The present cross-sectional study aims to evaluate the circulating concentration of 25-hydroxy vitamin D and the bone mineral density status of breast cancer patients and to study their relation to the treatment received and the stage of breast cancer.

Patients and Methods

Seventy-four female patients with breast cancer were randomly recruited from the oncology department of Saudi German Hospital during the period of April 2013 to April 2014. Complete history was obtained and rheumatological examination performed. Fifty-two age and sex matched healthy adult females were recruited as controls.

Exclusion criteria from the study involved active hyper- or hypoparathyroidism, uncontrolled thyroid disease, clinically relevant vitamin D deficiency, malabsorption syndromes, Paget’s disease, Cushing’s disease, pituitary diseases, bone diseases, renal dysfunction, other malignancies, and diseases known to influence bone metabolism. Patients on long-term treatment with anti-convulsants, anti-coagulants, sodium fluoride, calcium supplements, and bisphosphonates were excluded from this study. The study was performed in accordance with the Declaration of Helsinki, and all women patients gave written consent for enrollment in the study.

Biochemical analysis: All patients and controls were required to provide a full history and undergo a clinical examination. Non-fasting venous samples were separated and stored at -80 °C. Assays were performed for the serum alkaline phosphatase, serum phosphate and serum calcium levels. Serum 25-hydroxy vitamin D level: was measured using ELISA kit (Eagle Biosciences, Inc., 20A Northwest Blvd., Suite 112, Nashua, NH 03063 north of Boston, MA, USA); sensitivity of the kit was 0.02 pico mole/l; Intra-assay and inter-assay coefficient of variation (CV) were 3.2% and 8.6%.

Dual energy X-ray absorptiometry (DXA): was performed to assess bone mineral density (BMD) status for the hips, forearms, and spines of all participants. Patients were considered to have osteopenia if their adjusted T scores were -1.0 to -2.5 and osteoporosis if their adjusted T scores were ≤-2.5 at any measurement site [21].

Statistical analysis of data was performed with a statistical package for the social sciences (SPSS) version 21. Data were presented as mean ± standard deviation or number and percentage as appropriate. Chi-square test was used for analysis of non-parametric data and unpaired Student’s t-test, ANOVA, and linear correlation were used for parametric data. A p-value of less than 0.05 was considered significant.
Results

Thirty breast cancer patients were included with a mean age of 46.3±6.3 years. Thirty age and sex matched controls had a mean age of 48.1±9.66 years. None of the patients or control were smoking. Twenty-one patients were menstruating (5 with irregular menses) and 9 postmenopausal. The age, laboratory and DXA results of the cancer patients and controls are shown in Table 1. Breast cancer was unilateral in all the patients (10 on the right side and 64 on the left). In cancer breast cases, there was osteopenia at the hip region in 14 (18.9%) patients, at the forearm in 20 (27%) and at the spine in 14 (18.9%) while osteoporosis was present in 8 (10.8%) patients at the hip, 2 (2.7%) at the forearm and in 9 (12.2%) at the spine.

Twelve (16.22%) patients received chemotherapy only, another 12 (16.22%) received chemotherapy and hormonal therapy, 22 (29.70%) received chemotherapy and radiotherapy, and 28 (37.80%) received chemotherapy, hormonal therapy, and radiotherapy. The chemotherapy regimens used were (5-fluorouracil, doxorubicin and cyclophosphamide) for 6 cycles, or (docetaxel, doxorubicin and cyclophosphamide) for 6 cycles, or sequential (doxorubicin and cyclophosphamide) for 4 cycles then paclitaxel for 4 cycles. The dose of 5-fluorouracil was 600 mg/m2, doxorubicin 60mg/m2, cyclophosphamide 600 mg/m2, docetaxel 75 mg/m2, and paclitaxel 175mg/m2. Hormonal treatment included aromatase inhibitors (AIs) such as letrozole 2.5mg daily, anastrozole 1mg daily, exemestene 25mg daily and the anti-estrogen tamoxifen 10mg bid daily or a luteinizing hormone-releasing hormone (LHRH) agonist goserelin 3.6mg SC monthly. All patients underwent tumor resection, completed chemotherapy and/or radiation therapy within one year of study entry, and had no evidence of residual disease.

Regarding stages of the disease, 2 cases (2.7%) were in stage I, 18 cases (24.3%) were in stage II, 40 (54.1%) were in stage III, and 14 (18.9%) were in stage IV.

On considering the treatment regimen received by the patients; in those receiving chemotherapy only (n=12) there was hip osteoporosis in 4 cases (33.3%), forearm osteopenia in 33.3% and spine osteopenia and osteoporosis detected in 4 patients each; in those receiving chemo and hormonal therapy (n=12), hip osteopenia was present in 6 (50%), forearm osteopenia found in 8 (66.7%), spine osteopenia and osteoporosis in 33.3% and 25% respectively; in those receiving chemo and radiotherapy (n=22) osteopenia and osteoporosis of the hip and spine were present in 9.1% of cases, forearm osteopenia was found in 18.2% while osteoporosis in 9.1%; and in those receiving chemo, hormonal and radiotherapy (n=28), hip osteopenia was present in 21.4% while forearm and spine osteopenia were present in 14.3%. Comparison of biochemical data and DXA score of breast cancer patients according to treatment regimen are presented in Table 2.

Table 1: Comparison between age, biochemical data and DXA score of control and breast cancer patients

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD (range)</th>
<th>Cancer breast (n = 74)</th>
<th>Control (n = 52)</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.3±6.3 (27-65)</td>
<td>48.1±9.66 (37-60)</td>
<td>-0.34</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Calcium (Ca)</td>
<td>9.1±0.7 (7.9-10.2)</td>
<td>9.1±0.7 (8.05-10.3)</td>
<td>0.08</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Phosphorus (P)</td>
<td>1.6±0.4 (0.9-2.5)</td>
<td>2.2±0.4 (1.6-2.8)</td>
<td>7.58</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>221.5±50 (139-3054)</td>
<td>188.2±48.9 (105-277)</td>
<td>-3.75</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>25-OH D (IU/L)</td>
<td>18.4±6.3 (7-33)</td>
<td>23.7±5.2 (17.9-34.6)</td>
<td>5.02</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>DXA score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td>-0.2±1.04 (-0.3 - 1)</td>
<td>0.3±0.47 (-0.7 - 0.9)</td>
<td>4.33</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Forearm</td>
<td>-0.1±1.05 (-0.2 - 1.7)</td>
<td>-0.1±0.63 (-0.9 - 0.9)</td>
<td>2.07</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Spine</td>
<td>-0.2±1.07 (-2.8 - 1.5)</td>
<td>-0.6±0.5 (-0.8 - 0.8)</td>
<td>3.21</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Ca: Calcium, P: Phosphorus, ALP: Alkaline phosphatase, 25-OH D: 25-hydroxy vitamin D, DXA: Dual energy x-ray absorptiometry. Bold values are significantly different at p<0.05
scores compared to the control group. There was a marked sig-
cancer patients is severely compromised, as indicated by DXA
of the present study have proven that the bone status of breast
vitamin D source and hormone receptor status [31]. The results
better understand potential differences in breast cancer risk by
for the prevention of cancer [30]. Future research is needed to
regarding the benefits or harms of vitamin D supplementation
ever, evidence is not sufficiently robust to draw conclusions
D and calcium supplementation can reduce fracture risk. How
showed only a borderline association [29]. Combined vitamin
levels and breast cancer risk was seen [26-28], and one study
studies where no association between 25-hydroxy vitamin D
trations [25]. On the other hand, there were three comparable
found with the increase in serum 25 (OH) vitamin D3 concen-
phosphorus and 25-hydroxy vitamin D in breast cancer patients

tive vitamin D from circulating precursors, makes the effect of
Vitamin D has also been reported to have anticancer activities
against many cancer types, including breast cancer. The break-
through that breast epithelial cells can locally manufacture ac-
tive vitamin D from circulating precursors, makes the effect of
vitamin D in breast cancer biologically conceivable [22]. In the
present study, there was a significant decrease in serum phosph-
ors and 25-hydroxy vitamin D in breast cancer patients
compared to healthy controls. These results were in accord-
ance with the results of Crew et al., who stated that there is an
“inverse association identified between 25-hydroxy vitamin D
levels and breast cancer development” [23]. This is in harmony
and serum phosphorus (r=-0.26, p=0.03) as well as with the
DXA of hip (r=-0.3, p=0.01) and spine (r=-0.41, p=0.0001).

Discussion

Vitamin D has also been reported to have anticancer activities
against many cancer types, including breast cancer. The break-
through that breast epithelial cells can locally manufacture ac-
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and serum phosphorus (r=-0.26, p=0.03) as well as with the
DXA of hip (r=-0.3, p=0.01) and spine (r=-0.41, p=0.0001).

A significant correlation was found between the grade of tumor
and serum phosphorus (r=0.231, p=0.048) while negative cor-
relations were found between tumor grading with the serum
25- hydroxyl vitamin D level (r=-0.26, p=0.03) as well as with the
DXA of hip (r=-0.3, p=0.01) and spine (r=-0.41, p=0.0001).

Table 2: Comparison of biochemical data and DXA score of breast cancer patients according to treatment regimen

<table>
<thead>
<tr>
<th></th>
<th>CT only</th>
<th>CT &amp; HT</th>
<th>CT &amp; RT</th>
<th>CT, HT &amp; RT</th>
<th>ANOVA F</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biochemical data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>9.4 ± 0.5</td>
<td>9.3 ± 0.3</td>
<td>9.1 ± 0.9</td>
<td>8.8 ± 0.7</td>
<td>3.2</td>
</tr>
<tr>
<td>P (mg/dl)</td>
<td>1.2 ± 0.2</td>
<td>1.5 ± 0.1</td>
<td>1.7 ± 0.6</td>
<td>1.8 ± 0.4</td>
<td>6.1</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>203.3 ± 4.1</td>
<td>255.8 ± 37.6</td>
<td>208.3 ± 49.6</td>
<td>226 ± 56.6</td>
<td>3.3</td>
</tr>
<tr>
<td>25-OH D (IU/L)</td>
<td>15.3 ± 6.1</td>
<td>18.8 ± 1.3</td>
<td>17.67 ± 6.6</td>
<td>20.1 ± 6.95</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>DXA score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td>-0.8 ± 1.5</td>
<td>-1.1 ± 1.6</td>
<td>-0.3 ± 1.1</td>
<td>-0.2 ± 0.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Forearm</td>
<td>-0.8 ± 0.9</td>
<td>-0.8 ± 1.5</td>
<td>-0.3 ± 1.2</td>
<td>-0.2 ± 0.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Spine</td>
<td>-0.9 ± 1.6</td>
<td>-0.96 ± 1.3</td>
<td>-0.3 ± 1.04</td>
<td>-0.2 ± 0.8</td>
<td>1.5</td>
</tr>
</tbody>
</table>

CT: Chemotherapy, HT: Hormonal therapy, RT: Radiotherapy, Ca: Calcium, P: Phosphorus, ALP: Alkaline phosphatase, 25-OH D: 25-hydroxy vitamin D, DXA: Dual energy x-ray absorptiometry. Bold values are significantly different at p<0.05.
significantly reduced BMD DXA t score of the spine and forearm in patients with malignancy [36]. Moreover, in a previous study, patients receiving AIs were found to be at a higher risk of developing osteoporosis compared to normal subjects [37].

**Conclusion**

In conclusion, the vitamin D levels and BMD of the hip, forearms and spine are obviously reduced in breast cancer patients. The sub-clinically detected hypovitaminosis D, osteoporosis and osteopenia all throw light on the importance of offering calcium and vitamin D supplements to breast cancer patients. It is further recommended that breast cancer patients have a DXA scan performed at baseline and repeatedly on a yearly basis. Conducting the study longitudinally on a larger scale of patients is required to confirm our results.

**References**


Pregnancies Complicated by Severe Autoimmune Thrombocytopenic Purpura

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ABSTRACT

Objectives: To assess pregnancy course and perinatal bleeding in women with severe autoimmune thrombocytopenic purpura.

Material and methods: We collected data of 38 pregnancies in 24 women, who were on treatment for autoimmune thrombocytopenic purpura early in pregnancy. Indication for treatment was platelets count 50,000/mm³ or less. We looked for premature rupture of membranes, premature delivery, intrauterine growth restriction and significant blood loss at delivery. Those women were the study group, (group 1). The same variables were looked for in 100 healthy pregnancies taken as control (group 2). Data was compared between the two groups. Information was obtained prospectively from the woman’s follow up visits at maternal medicine clinic, King Hussein Medical Center as well as data gathered from women with previous pregnancies complicated by autoimmune thrombocytopenia. Women who had thrombocytopenia secondary to other conditions such as systemic lupus, bone marrow diseases and other causes, were not included in the study.

Results: The study group 1 had nine premature ruptures of membranes in 38 pregnancies, whereas only ten women ruptured their membranes out of 100 in control group 2 with an odds ratio 2.9. Four women had significant blood loss at delivery in group 1 and eight women in group 2 which presents marginal increase for group 1 (odds ratio 1.3). No increase in growth restricted babies nor in premature delivery was noticed.

Conclusion: Pregnant women with autoimmune thrombocytopenic purpura on treatment, have significant higher risk to rupture their membranes prematurely. No increase in growth restricted babies and premature deliveries. With good care they can deliver safely with minimum hazard of bleeding.

Key words: pregnancy, complication, thrombocytopenia, bleeding
Introduction

Pregnant women with thrombocytopenia are not infrequently met at antenatal clinics (7-10%) (1). Some of them are accidentally discovered during routine blood test. Pregnancy induced thrombocytopenia is the most encountered cause related to pregnancy (2), whereas Idiopathic thrombocytopenic purpura is the most encountered cause that is unrelated to pregnancy (3). Platelets count was found normally lower in pregnancy and decreases as pregnancy advances (4). In one study (5), back in 2001, it was found that platelets function in women with pregnancy induced thrombocytopenia was preserved. A recent study (6) emphasized on the increase in platelets aggregation in pregnant women when compared to non-pregnancy state. Pregnancy course and the complications that may be encountered are attributed to the disease itself or to drugs used to ameliorate the disease. Studies are conducted to minimize the risk of thrombocytopenia on pregnant women and on the developing fetus. Management needs to balance between the hazard of low platelets count and the risk of drugs used on the mother and the fetus. When medication is needed, corticosteroids are first line of treatment (7). It is known for its side effect on blood pressure, glucose tolerance and immunity among others (8). Other immunomodulating drugs are used which are not risk free.

It may be difficult to distinguish between gestational induced thrombocytopenia and ATP when first recognized during pregnancy (9), nevertheless, gestation induced thrombocytopenia is known to have mild disease course. Actual platelets count has to be looked for sometimes when platelets clumps are formed. Tubes with different anticoagulant media are used. Sodium citrate, heparin Ethylenediaminetetraacetic acid tubes are dispatched to the lab, platelets count can be performed manually when suspicion of clumping or agglutination arises (10).

The aim of our study is to look for pregnancy course in women with severe autoimmun thrombocytopenia, in regard to premature rupture of membranes, to fetal body weight at delivery, prematurity and peripartum bleeding.

In our study we followed the course of pregnancies complicated by severe autoimmune thrombocytopenia, which were diagnosed prior to pregnancy, or first discovered during gestation. Severe thrombocytopenia is when platelets count decreases to less than 50,000 x 10^3/L (11).

Methods

24 pregnant women with 38 pregnancies diagnosed with severe autoimmune thrombocytopenic purpura were considered in the study; they were taken as study group and labeled as (group one). Another 100 women with normal course pregnancy and normal platelets count were also included in the study as control group and labeled as (group two). Severe thrombocytopenia is when platelets count decreases to less than 50,000/mm3. They were followed up at maternal medicine clinic, Obstetrics department. Data were obtained prospectively from patients’ follow up records and retrospectively of previous pregnancy and post natal visits. All women were on oral steroids; some of them had other immune modulating drugs added. An oral steroid (Prednisolone) was use in a dose of 20 to 60 mg. Azathioprine in doses 50 to 100 mg was added in 4 women. Two women received intravenous immunoglobulin for resistant disease at gestational age 28 for one of them and at 30 weeks for the second patient. The aim of treatment was to keep platelets count at or above 40,000/mm3. Citrate, heparin or ethylene diamine tetra acetic acid tubes were dispatched to the laboratory. Manual count was also requested when suspicion arises. No considerable spontaneous bleeding was met and thus no blood transfusion was considered for any patient before delivery. Minor epistaxis resolved by local hemostatic care. Platelets transfusion was considered only at delivery or before surgery to raise platelets count up to 50,000/mm3.

The course of pregnancy and bleeding at delivery was studied and compared between the two groups. We looked at premature rupture of membranes, premature delivery, babies small for gestation age and amount of blood loss at delivery.

Premature rupture of membranes was defined as amniotic fluid passage before onset of labour at any gestational age. Deliveries before 37 weeks completed of gestation were taken as premature delivery. Fetal body weight at delivery at or less than the 10th centile was considered small for gestational age. Blood loss was considered significant when hemoglobin concentration decreases by 2gr/dl or more for vaginal delivery and 3gr/dl or more after operative delivery. Caesarean section was conducted for obstetric reasons or as maternal request after counseling the family.

Using MedCalc software, Odds ratio and confidential intervals and p-value were calculated.

Results

38 pregnancies with severe thrombocytopenia were included in the study, all of them were on oral Prednisolone 20 mg and up to 60 mg. Azathioprine was added in a dose of 50 up to 100 mg for 4 women who were resistant to Prednisolone alone. Two cases did not respond to Prednisolone and Azathioprine; they received Intravenous immunoglobulin and 8 women needed platelets transfusion when in labour or before operative delivery.

Nine women in study group ruptured their membranes before the onset of labour (23.6%), four had significant bleeding (10%), five delivered babies at or below the 10th centile (13%), and four had premature deliveries before 37 weeks completed (10%).

In the control group the results were 10 (10%), 8(8%), 12(12%), 11(11%) respectively, (Table 1).
Table 1: Comparison in pregnancy course and peripartum bleeding between groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Increased blood loss</th>
<th>SGA 10th percentile</th>
<th>Prematurity 37th week</th>
<th>SRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>N=38</td>
<td>4 (10)</td>
<td>5 (13%)</td>
<td>4</td>
</tr>
<tr>
<td>Group 2</td>
<td>N=100</td>
<td>8 (8%)</td>
<td>12 (12%)</td>
<td>11</td>
</tr>
<tr>
<td>OR 95% CI</td>
<td>1.35</td>
<td>0.38-4.78</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>P-Value</td>
<td>0.6 n/s</td>
<td>n/s</td>
<td>n/s</td>
<td>0.04</td>
</tr>
</tbody>
</table>

n/s = not significant

Spontaneous rupture of membranes was significantly increased in women with severe thrombocytopenia on treatment than in women with no steroid treatment and normal platelets with an odds ratio of 2.9, (95% CI 1.03-7.53).

There was minimal increase in peripartum bleeding, (OR 1.3, 95% CI 0.3-4.7); it was not statistically significant. No blood replacement was needed.

No difference was found in the rates of premature deliveries or in small for gestation babies between the two groups.

Discussion

Women with thrombocytopenia present a special challenge to obstetricians in the fertility period. Bleeding that may occur during pregnancy and delivery due to obstetric reasons has particular hazard when thrombocytopenia is superimposed. The Obstetrician has to place platelet count at safe levels to ensure maternal health. Drugs used in the aim of achieving this goal may not be risk free. In our study we tried to estimate the hazard of medication used in managing thrombocytopenia in pregnancy.

Prednisolone, a synthetic corticosteroid is the first line and main stay treatment. It was found not to cause major fetal abnormalities (12,13). Nevertheless the risk of premature rupture of membranes has been recognized by different studies(14). In accordance with those studies, we found that premature rupture of membranes occurred more frequent in thrombocytopenic women on Prednisolone. It is difficult to establish if the increase in premature rupture of membranes is exclusively due to steroids treatment or thrombocytopenia per se presents an independent risk factor.

Blood loss at delivery was marginally increased in women with thrombocytopenia. This emphasises the fact that platelets function is preserved, and the hazard of peripartum bleeding is not immense, particularly when appropriately managed.

Excluding cases with premature rupture of membranes, premature delivery was not increased in our study. This leads to the conclusion that thrombocytopenia is not a direct risk factor for premature delivery.

The risk of small for gestation babies at delivery was not increased also. This highlights the normal fetal growth pattern, normal oxygenation and nutrition.

Conclusion

Our results suggest that pregnant women with severe autoimmune thrombocytopenia on treatment have an increased risk to rupture their membranes prematurely. This may be due to medications used in managing the condition, or due to the disease itself. Risk of bleeding may exist, but with appropriate care and management it is of low risk. Fetal growth and premature deliveries are not more likely in isolation of premature rupture of membranes.

Number of subjects represented a limitation to the study; more studies in larger numbers are needed to verify those results.

References


Presenting Case

Mrs. Fatima Hussain is 76. She has been a long-standing patient of the practice and has been troubled by mild angina, hypertension and borderline glucose colectomy for diverticular disease. You are aware that she has renal impairment.

Six months ago Fatima’s serum creatinine was checked when she presented with a small AIM - it was 230 umol/L. At that time she was admitted to hospital for her AIM and the hospital doctors said there were no reversible causes of her renal failure. Her MSU and urine dipstick were normal.

She presents now with increasing angina, which she develops on walking about 30-40 metres, or up the four back steps at her housing unit.

Question 1
The following are possible causes of renal failure: Select the most likely cause in Mrs Hussain’s case.

Chronic glomerulonephritis
Renal artery stenosis
Diabetes
Long-standing hypertension
Polycystic kidneys

(See next page for Author’s answers)
Author’s Answers and feedback on Question 1

Chronic glomerulonephritis
The authors disagree.
Chronic glomerulonephritis is unlikely, given the normal urinary findings. There is virtually always some proteinuria in chronic GN and often haematuria as well.

Renal artery stenosis
The authors disagree.
Renal artery stenosis is half right! For renal artery stenosis to cause renal failure, there must be bilateral disease. Nevertheless, bilateral renal artery stenosis is possible in women of this age, particularly as she has other evidence of vascular disease.

Diabetes
The authors disagree.
Diabetes with diabetic nephropathy is unlikely if there is no proteinuria on dipstick. In the situation of advanced diabetic nephropathy with a creatinine of this level, there will always be significant proteinuria, often greater than 3 gm/day. Supporting evidence for diabetic nephropathy would be the presence of diabetic proliferative retinopathy.

Long-standing hypertension
The authors agree.
Long-standing hypertension with associated nephrosclerosis (so called ‘benign’ nephrosclerosis) is the most likely cause of Mrs. Hussain’s renal failure. Typically this has blameless urinary findings, sometimes with low-grade proteinuria. There is usually a long history of hypertension and often vascular disease. In some respects this entity is ‘advanced aging’ of the kidney.

Polycystic kidneys
The authors disagree.
Polycystic kidneys would be unlikely - they should have been noticed clinically by now, although some patients with polycystic kidneys may develop renal failure late in life. Nevertheless, they usually have obvious enlarged kidneys prior to that.

Continuing history
You are unhappy with Mrs. Hussain’s angina and notice that she looks a little pale. You discover that her haemoglobin is 89 gm/l (or 8.9 gm/dl). There is no history of bleeding, altered bowel motions nor dyspepsia. Mrs. Hussain had a hysterectomy many years ago. There is no spleen palpable, nor any lymphadenopathy and the rest of the examination is unremarkable.

Question 2
You decide to investigate the anaemia. From the following list of tests, select the ONE most useful test
U+E’s, Cr
Serum iron and ferritin
FBE with film
Reticulocyte count
B12 and Folate levels
Serum protein immuno-electropheresis
Author’s Answers and feedback on Question 2

U+E’s, CR
The authors disagree.
This would give some indication as to whether her renal function had deteriorated further. Renal failure causes anaemia.

Serum iron and ferritin
The authors disagree.
Iron deficiency is the commonest cause of anaemia in the community, usually with loss of blood from the GIT. This would be an appropriate test but not the ONE most useful.

FBE with film
The authors agree.
This is the best test- the film will tell you the red cell size and morphology, suggesting therefore whether any of the following are likely: iron deficiency (small cells), folate deficiency (large cells), or B12 deficiency (large cells). Other forms of anaemia may also be suggested; the anaemia of chronic renal failure is normochromic, normocytic (normal size cells).

Reticulocyte count
The authors disagree.
An elevated reticulocyte count would suggest either recent bleeding or haemolysis, and this could be useful.

B12 and Folate levels
The authors disagree.
Deficiency of these vitamins is less common and probably these tests should only be ordered on the basis of macrocytosis on the blood film.

Serum protein immuno-electrophoresis
The authors disagree.
This will detect myeloma. This is not uncommon in elderly patients but a hint might be pancytopenia on the blood film rather than just anaemia, although this is not absolute. Probably best as a second line test.

Continuing history
You make a further appointment for Mrs. Hussain to return in a few days for test results.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat Hb</td>
<td>88gm/l</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>290 umol/l</td>
</tr>
<tr>
<td>Serum Fe</td>
<td>Normal</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>Normal</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>Low</td>
</tr>
<tr>
<td>Blood film</td>
<td>Normochromic, normocytic</td>
</tr>
</tbody>
</table>
Question 3
Which of the following statements will you give to Mrs. Hussain concerning the meaning of these results?

Select your preferred choice.

- “You have mild anaemia which is measured at only 88% of normal”.
- “You have anaemia consistent with blood loss from diverticulitis”.
- “Your anaemia is called the anaemia of chronic disease”.
- “You will need to take Fe tablets for the rest of your life”.

Author’s Answers and feedback on Question 3

“You have mild anaemia which is measured at only 88% of normal.”
The authors disagree.
The normal Hb level for women is greater than 120 gm/l, making a Hb of 88 more severe than “88%”. Most patients will be symptomatic at a Hb of 88 and many will require treatment.

“You have anaemia consistent with blood loss from diverticulitis.”
The authors disagree.
The normochromic, normocytic pattern is not consistent with blood loss. In addition, diverticular disease usually doesn’t cause unnoticed blood loss but rather tends to be intermittent but heavy in nature.

“You are anaemia is called the anaemia of chronic disease.”
The authors agree.
Mrs. Hussain almost certainly has the anaemia of chronic renal failure. The normochromic, normocytic pattern is consistent with this.

“You will need to take Fe tablets for the rest of your life.”
The authors disagree.
As this is not an iron deficient pattern, it would be wrong to suggest that iron tablets will be necessary. Iron may not help at all in this situation. A proviso is that most patients who go on to require erythropoietin do require a significant intake of iron.

Question 4
Which of the following decisions will you now make?

Select ONE only.
- Transfuse her two units of packed cells
- Nothing, apart from increasing her anti-anginals
- Refer her for dialysis
- Refer her for erythropoietin therapy
Author’s Answers and feedback on Question 4

Transfuse her two units of packed cells
The authors disagree.
This may well improve her angina but volume overload is a risk. However, she is likely to become anaemic again over the ensuing weeks and will need repeated transfusions. Transfusions will also ‘turn off’ her endogenous erythropoietin, thus increasing her transfusion dependence.

Nothing, apart from increasing her anti-anginals
The authors disagree.
Anaemia is one of the ‘curable’ causes of angina and increases in anginal therapy may not be required if anaemia is improved.

Refer her for dialysis
The authors disagree.
Mrs. Hussain may not be considered a good dialysis candidate. She is elderly and has significant ischaemic heart disease. She is not likely to be offered dialysis - her heart disease would make haemodialysis difficult and her past abdominal surgery means that peritoneal dialysis may not be possible. At this stage, she doesn’t require dialysis and dialysis would not correct her anaemia.

Refer her for erythropoietin therapy
The authors agree.
This is a good option. Erythropoietin will correct her anaemia and probably improve her angina and general well being.