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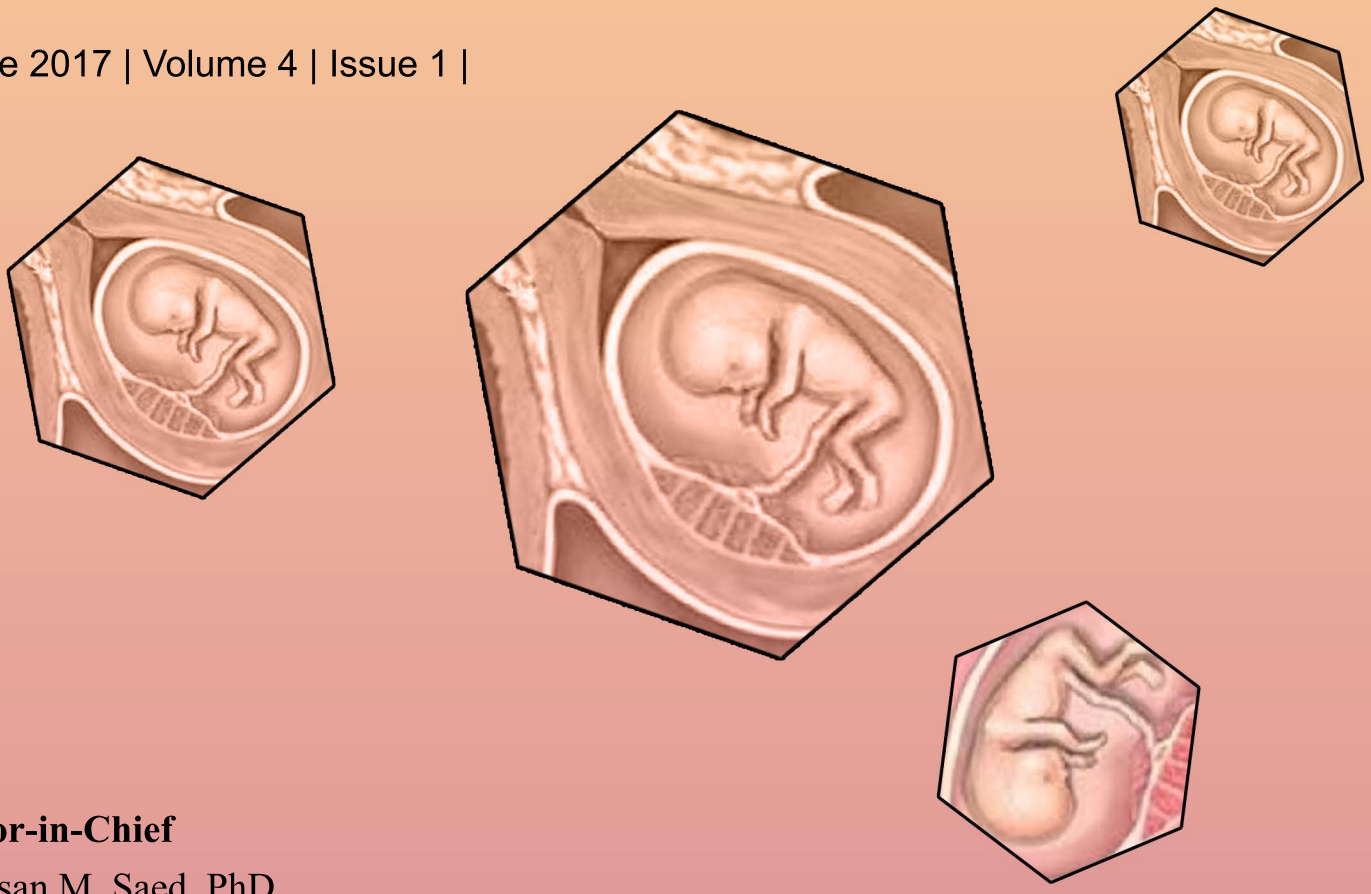

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A Novel Contributor to Endometrial Receptivity: Endometrial Microbiota

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In the recent years, our knowledge about human reproductive system has increased with the development of assisted reproductive technologies; however, embryo implantation rate is still around 25-30%.[1] Embryo implantation depends on the quality of the embryo, endometrial receptivity and the embryo/endometrial interface.[2] The onset of implantation is a successful concurrence of 2 different processes; embryo development and endometrial differentiation. Therefore, synchronization between development of a good quality embryo and receptive endometrium is paramount for the success of embryo implantation and ongoing pregnancy.[2,3] The association between embryo and receptive endometrium during implantation is not fully understood yet, because *in vivo* studies about implantation are scarce due to ethical and technical problems. So our knowledge about implantation is mostly derived from animal studies.[4,5]

Microbiota which was fully defined in 2001 is regarded as the second genome, and its importance in reproductive system has newly understood.[6-9] Microbiota is a source of genetic diversity and is important for normal immune system, metabolism and behavior of the disease.[10] Microbiota inhabits different systems of the body and there is a synergistic interaction between microbiota and its host.[10] Due to these known synergistic effects, microbiota transplantation has been used as a treatment for recurrent *Clostridium difficile* infection which may be difficult to manage with conventional antibiotic therapies. Fecal microbiota transplantation from a healthy person to the patient restores the gut microbiota to a healthy state.[11,12]

Endometrial receptivity is regulated by synchronization of different cell types and several factors such as luminal and glandular epithelium, cytokines, growth factors, proteases, glucose, hormones and enzymes.[2,3] Recent research has also revealed the importance of endometrial microbiota and its possible impact in endometrial receptivity.[13,14] Until recently, endometrium was classically considered a sterile cavity and when the reproductive system microbiota was considered, vaginal microbiota came to mind.[15] However, new techniques and technologies such as microarrays, DNA fingerprinting, and targeted or whole genome sequencing have empowered the field of metagenomics and have begun to change the way we think of reproductive system microbiota.[16] With help of these innovations, identification of microorganisms in uterine cavity of asymptomatic patients undergoing hysterectomy for benign indications confirmed that the uterine cavity is not sterile and endometrium has an own microbiota such as *Gardnerella vaginalis*, *Lactobacillus* spp., *Enterobacter* spp. and *Mycoplasma hominis* and is independent from hormonal regulation.[14] In the future, endometrial microbiota transplantation may be used for recurrent implantation failure patients.

Recent studies reported that non lactobacillus microbiota domination in endometrial cavities is strongly correlated with failure of implantation as compared to lactobacillus dominated endometrial microbiota.[14,17] Because balance in inflammatory factors is important for regulation of the adhesion of the blastocyst to the epithelial endometrial wall, non-lactobacillus dominated microbiota may cause inflammation in the uterine cavity and impair endometrial receptivity.[14] We need new studies focusing on the interaction between endometrial microbiota and receptivity.

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As a result, a human endometrial microbiota exists and is independent of hormonal regulation. Non-Lactobacillus dominant endometrial microbiota impairs endometrial receptivity and may result in implantation failure and pregnancy loss but lactobacillus dominancy is a supporter of healthy reproductive system. Now, we have to know that endometrial receptivity is not only under control of the morphological and molecular factors but endometrial microbiata has substantial functions for endometrial integrity and successful implantation. It is time to consider microorganisms not only as enemies but also as allies in reproductive medicine.

CONFLICTS OF INTEREST

None of the authors have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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Post-Operative Outcomes of Oxidized Regenerated Cellulose Use in Women Undergoing Cesarean Delivery

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ABSTRACT

Introduction: In spite of careful technique, bleeding may continue to occur at time of surgery. Absorbable hemostatic agents have been developed in order to control hemorrhage. However, no study to date has investigated post-operative outcomes when oxidized regenerated cellulose is used routinely at time of cesarean delivery.
Objective: To assess post-operative outcomes associated with routine use of oxidized regenerated cellulose at the time of cesarean delivery
Methods: Retrospective chart review of cesarean deliveries divided into two groups: Those in which oxidized regenerated cellulose was used and those in which it wasn't. Following data were obtained: Maternal baseline characteristics, estimated blood loss, pre- and post-operative complete blood counts and incidence of fever and post-operative abscess. Student *t*-test and Chi-square were used for statistical analysis.
Results: Of 155 patients, oxidized cellulose was used in 77 (50%). Baseline characteristics between groups were similar. Mean estimated blood loss was not significantly different between groups (803 mL *vs* 800 mL, p=0.32). Increase in pre- and post-operative white blood cell count (3.5 *vs.* 3.3, p=0.65) and decreases in pre- and post-operative hemoglobin (1.7 *vs.* 1.9, p=0.21) and hematocrit (4.5 *vs.* 5.1, p=0.29) were not significantly different between groups. However, there was a significantly increased incidence of fever in the group in which oxidized cellulose was used (13.0% *vs.* 3.9%, p<0.05). Abscess formation did not occur in either group.
Conclusion: Oxidized regenerated cellulose use was associated with an increased incidence of post-operative fever without significantly affecting changes in pre- and post-operative hemoglobin and hematocrit.

KEYWORDS: Oxidized regenerated cellulose; Cesarean section; Post-operative outcome.

INTRODUCTION

Cesarean delivery is one of the most commonly performed surgical procedures in women. The national cesarean delivery rate is approximately 30%.[1] At the time of cesarean, careful surgical technique and dissection is essential in avoiding bleeding, a principle that is fundamental to all surgical approaches. However, bleeding may continue to occur in spite of these efforts and has led to the development of absorbable hemostatic agents in order to control hemorrhage. Literature within the hepatic and spinal surgery fields has supported the efficacy of these agents.[2-3] Oxidized-regenerated cellulose and microfibrillar-collagen have been used at the time of cesarean delivery. The mechanism by which these agents accelerate clotting is not completely understood but it is theorized that a physical effect and/or an alteration of normal physiologic processes may be at play.[4] These agents are typically placed over the uterine incision closure at the time of cesarean delivery in order to provide hemostasis in addition to conventional methods using suture. In spite of its benefits, use of absorbable hemostatic agents may not necessarily be without risk and may cause a probiotic microenvironment that can contribute to bacterial proliferation.[5-6] A study performed by Anderson et al[7] investigated the association of gelatin-thrombin matrix use and abscess formation in patients undergoing hysterectomy and found that

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nine patients developed an abscess with gelatin-thrombin use as opposed to only two patients who developed an abscess in the absence of gelatin-thrombin use. However, no study to date has assessed the association between routine absorbable hemostatic agent use, as a means of preventing post-operative bleeding, and post-operative fever and abscess formation in women undergoing cesarean delivery. Hence, the purpose of this study was to assess post-operative outcomes associated with routine use of oxidized regenerated cellulose at the time of cesarean delivery.

METHODS

This study was an IRB-approved retrospective cohort study. Inclusion criteria consisted of those who underwent cesarean delivery and received their post-operative care at Hofstra University-Northwell Health System-Staten Island University Hospital between 2013 and 2015. Exclusion criteria consisted of those with a documented estimated blood loss of greater than 1000 milliliters and those who underwent procedures in addition to cesarean delivery such as bilateral tubal ligation, myomectomy and lysis of adhesions. Charts of 155 patients were reviewed. The following information were obtained: Age, parity, gestational age at time of cesarean delivery, body mass index, number of prior cesarean deliveries, estimated blood loss, incidence of administration of pre- and post-operative antibiotics, pre- and post-operative complete blood counts and incidence of post-operative fever and abscess. If oxidized regenerated cellulose was used at the time of cesarean, it was placed over the uterine incision after uterine incision closure. All patients received pre-operative antibiotics and received the same pre-operative antibiotic post-operatively for up to 24 hours after surgery, unless the provider determined that the post-operative antibiotic regimen should be changed. Student's *t*-test and Chi square were performed on the relevant data.

RESULTS

No significant differences were noted between the groups with respect to maternal age, parity, gestational age at time of delivery, body mass index and number of prior cesarean deliveries (Table 1). There was no significant difference between the groups with choices of pre-operative and post-operative antibiotic administration.

Mean estimated blood loss did not differ significantly between the group in which oxidized regenerated cellulose and the group in which it wasn't (803±34 mL *vs.* 800±0 mL, p=0.32). There were no significant differences between the groups with respect to preoperative white blood cell count, post-operative white blood cell count, preoperative hemoglobin and hematocrit and post-operative hemoglobin and hematocrit (Table 2). However, 13.0% of those in the group in which oxidized regenerated cellulose was used experienced post-operative fever *versus* 3.9% in the group in which it was not used. There were no cases of abscess formation.

DISCUSSION

Over the past decade, the use of hemostatic agents to control bleeding has increased significantly. These hemostatic agents can be divided into physical, absorbable, biologic and synthetic agents.[8] Oxidized cellulose was first introduced in 1942[9] and oxidized regenerated cellulose was launched in 1960. Oxidized regenerated cellulose is created by decomposing wood pulp and then regenerating the cellulose by manufacturing continuous cellulose fibers. This material has been branded as Surgicel® by Johnson & Johnson® and is used as a knitted fabric that can be cut to match the size of the area that needs hemostasis. Additionally, it does not stick to instruments, thus facilitating easier handling.

Table 1: Baseline Characteristics.

	Cellulose used (n=77)	Cellulose not used (n= 78)	*p* value
Age	31.4±6.4	30.6±5.7	0.46
Parity	1.2±1	1.0±1.0	0.23
Gestational Age	39±2.3	38.7±2.3	0.56
Body Mass Index	28.9±6.8	27.6±7.8	0.30
Number of prior cesarean deliveries			
0	30	35	0.46
1	30	28	0.16
2	10	12	0.67
3	5	3	0.46
4	2	0	0.15
Pre-operative antibiotics			
Cefazolin	72	73	0.98
Gentamycin/Clindamycin	5	3	0.46
Vancomycin	0	2	0.16
Post-operative antibiotics			
Cefazolin	70	73	0.53
Gentamycin/Clindamycin	5	3	0.46
Ampicillin/Gentamycin/Clindamycin	2	0	0.15
Vancomycin	0	2	0.16

Age, parity and gestational age are presented as mean±standard deviation. For number of prior cesarean deliveries and antibiotics, the number of patients per patient characteristic is indicated.

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Table 2: Operative Outcomes

	Cellulose used (n= 77)	Cellulose used (n= 78)	*p* value
Pre-operative white blood cell count	10.4±3.5	10.8±3.5	0.35
Post-operative white blood cell count	13.8±4.9	14.0±4.2	0.72
Change between pre- and post-operative white blood count	3.5±4.0	3.3±3.3	0.65
Pre-operative hemoglobin	12.1±1.2	12.1±1.2	0.80
Post-operative hemoglobin	10.4±1.5	10.2±1.3	0.44
Change between pre- and post-operative hemoglobin	1.7±1.2	1.9±0.9	0.21
Pre-operative hematocrit	36.2±3.1	36.0±3.0	0.69
Post-operative hematocrit	31.6±4.0	30.9±3.4	0.22
Change between pre- and post-operative hematocrit	4.5±3.4	5.1±3.0	0.29
Incidence of post-operative fever	10 (13.0%)	3 (3.9%)	$p<0.05$

All above are expressed as mean±standard deviation with exception of incidence of post-operative fever which is expressed as number of patients (percentage).

This hemostatic agent is absorbable and belongs to the same category as gelatin thrombin matrix and microfibrillar collagen. It is not completely clear how oxidized regenerated cellulose but several mechanisms have been theorized. As oxidized regenerated cellulose has a low pH, it may cause red blood cell lysis which may trigger hematin formation thus accelerating clotting with the help of normal physiologic processes. However, the acidic nature of oxidized regenerated cellulose may increase inflammation in surrounding tissue and delay wound healing.[10] Oxidized regenerated cellulose absorption typically lasts between two and six weeks but histologic evidence of oxidized cellulose fibers several years after cardiac surgery has been reported.[11] Research has been limited in regards to adverse effects of use of this agent but cases have been reported in which oxidized regenerated cellulose was used for hemorrhage control during thoractomy and the cellulose passed through the intervertebral foramen and caused cord compression.[12] No study till now has evaluated the use of oxidized regenerated cellulose in obstetric surgery.

In this study, it was found that the routine use of oxidized regenerated cellulose as a means to prevent hemorrhage was associated with a significantly increased incidence of post-operative fever without significantly attenuating the decrease in hemoglobin and hematocrit that occurs before and after surgery. There were no cases of abscess formation. Given the increase in incidence of post-operative fever, it was expected that there would be an association between use of oxidized regenerated cellulose and increase in white blood cell count before and after surgery. However, it was found that use of oxidized regenerated cellulose did not significantly elevate the increase in white blood cell count that occurs before and after surgery when compared to when oxidized regenerated cellulose wasn't used. Additionally, it was felt that in those instances in which oxidized regenerated cellulose was used and in which post-operative fever occurred that the fever was most likely attributed to use of the hemostatic agent as all other sources of post-operative fever were reliably ruled out. These other sources included deep venous thrombosis, pneumonia, urinary tract infection, mastitis and wound infection and were ruled out on the basis of unremarkable physical exam and imaging findings and negative blood and urine cultures.

There are weaknesses to this study. The retrospective nature and the small sample size diminishes the ability of these results to be generalized. Future directions for the research question at hand would be to perform a randomized, controlled study and to assess for incidence of post-operative fevers between the two groups in the absence of administration of post-operative antibiotics. Administration of post-operative antibiotics is a practice not performed at many institutions. Additionally, this study design would allow one to further clarify the relationship, if one does exist, between abscess formation and routine use of oxidized regenerated cellulose at the time of obstetric surgery and to truly elucidate a source, if any, for the increased incidence in post-operative fever that could have been masked by routine administration of antibiotics post-operatively in our institution. This is of critical importance, from a cost standpoint, as detection of post-operative fevers may trigger additional tests such as performance of chest x-rays, lower extremity Doppler and blood and urine cultures.

Nonetheless, this study does present data indicating that routine use of oxidized regenerated cellulose does not significantly attenuate the decrease in hemoglobin and hematocrit that occurs before and after surgery. Furthermore, routine use of oxidized regenerated cellulose at the time of cesarean delivery may be associated with an increased incidence of post-operative fever.

CONFLICTS OF INTEREST

The author has no conflict of interests to declare.

ETHICAL CONSIDERATION

Ethical approval was obtained for this retrospective chart review from the Institutional Review Board at Hofstra University–Northwell Health System–Staten Island University Hospital.

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Brief Report

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Pregnancy and Childbirth in Patients With Syndrome-Marfan

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ABSTRACT

Marfan syndrome (MFS) is an autosomal dominant condition with a reported incidence rate of 1 in 3000 to 5000 individuals. The majority of cases of MFS are caused by a mutation in the fibrillin-1 gene (FBN1). Transforming growth factor β (TGF-β) plays an important role in Marfan syndrome. The identification of the FBN-1 mutation will help identify potentially affected family members and promote prenatal diagnostic testing. β blockers decrease myocardial contractility and pulse pressure and may also improve the elastic properties of the aorta. Angiotensin II-receptor blockers attenuate the clinical manifestations of MFS.

KEY WORDS: Marfan syndrome; Aortic root enlargement; Ectopia lentis; Fibrillin-1; Beta blockers; Dural ectasia; Protrusio acetabuli.

INTRODUCTION

Marfan syndrome (MFS) is primarily inherited in an autosomal dominant manner and in some cases with a recessive manner, which affects one person in every 3000-5000 people in the general population.[1,2]

In the majority of patients due to gene mutations on fibrillin-1 [fibrillin-1 gene (FBN-1)], located in chromosome 15q-21.1q and comprises 65 exons.[2] Fibrillin-1 is an extracellular cysteine-rich protein that participates primarily in manufacturing and maintaining the structure of the microfibrils on the extracellular matrix of the elastic and non-elastic connective tissue.[3]

Mutations on the fibrillin-1 gene interrupt the normal structure of these micro fibrils thus inducing abnormal protein structure in which they participate. This may lead to an infringement of biomechanics (structure that can meet the functional role) connective tissue. The disturbance of homeostasis of connective tissue, for example, in blood vessel walls can cause strong solution of the connecting elastic fibers after intense expression of metalloproteinases (such as metalloproteinases -2 and -9) of the matrix, and increasing the hyaluronic acid can lead to degradation of these elastic fibers and other components of the matrix.[4] It is also reported to increase the activity of transforming growth factor-β [transforming growth factor beta (TGF-β)] interactions and loss of cell-matrix (cell-matrix interactions).[5]

Clinically the MFS may be manifested by a series of events from various organs and systems:

a. Dermal super elasticity transparent skin and stretch marks in skin areas such as the spine, the upper limbs, the inguinal regions and the leg.[6]

b. Regarding the musculoskeletal system general laxity of ligaments leading to hyper

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extensibility and instability with frequent joint dislocations and subluxations, prolapse of the femoral head,[7] valgus posterior segment combined with abduction of the anterior and shortening of the average part of the edge of the leg,[7] of the ends arachnodaktylia hands (especially long thin fingers) and the chest wall may be observed as distortion asymmetry and tropidoeidis (pectus carinatum) or funnel-shaped (pectus excavatum) thorax.[7] In the spine, scoliosis and spondylolisthesis are described.[8]

c. In the nervous system, dural ectasia (inflation of the bag of the dura and the vertebral canal together possibly swelling sheaths spinal nerves)[9] affects the spinal canal in all degrees of the spine, often in the lumbosacral region and can manifest with headache, back pain, damage of muscle power and limiting the sensation of the legs and pain in the anal region and external genital organs are deteriorating in the supine and enhances the prone (face down) bed.[10] Each patient escorted by Marfan syndrome with related clinical signs should be tested for possible dural ectasia using computational or MRI.[11]

d. In the eyes, ectopia (dislocation or abnormal axis) of the eye lens (ectopia lentis) the most common bilateral and symmetric but non-progressive[12,13] myopia, retinal detachment (possibly bilateral)[14,15] strabismus and glaucoma.[16]

e. In the cardiovascular system, involvement of the root of the aorta may result in aneurysmal dilatation/separating walls and insufficiency of the aortic valve.[17] Abdominal aortic root was reported in approximately 50% of children and 60%-80% adult patients, often combined with a failure of the aortic valve, and has been reported abdominal wall and the thoracic and abdominal aorta and the pulmonary artery (the root), the carotid and intracranial arteries.[18,19] The aorta showed a significant limitation in its luminal elasticity and durability, factors that increase with increasing age.[20-23] No significant correlation has been observed between aortic root infection with infection of other organs or systems such as the eye or the frame.[18] Cardiac involvement has also been observed with the most common mitral valve prolapse reported in 40%-54% of patients with Marfan syndrome.[24,25] Mitral valve infringement usually results in mild or moderate deficiency, although cases have been observed with severe infestation of spontaneous rupture of the tendon string.[24]

f. Respiratory system blisters (bullae) in the pulmonary parenchyma (most commonly detected in the upper lobes), rupture of which may lead to spontaneous pneumothorax.[1,6,26]

MRI provides the ability to detect the presence and extent of the aneurysm of the aorta and of these aneurysms relationship with the vessels of the aortic arch.[27]

Samples from the aortic root wall of tunica media reveal fragmentation of elastic fibers, cystic necrosis, fibrosis and loss of smooth muscle fibers that reflect the damage and repair process.[28-32]

Genetic testing on the fibrillin-1 gene mutations help in the detection of the affected patient's family members and promote prenatal diagnosis. The absence of mutations in a person suspected of MFS does not exclude the diagnosis, which should be based on medical history, clinical assessment and imaging evaluation. With regards to the relatives of patients with MFS the recommendations of the American College of Cardiology/ American Heart Association/American Association for Thoracic Surgery- 2010 state that[33]:

a. First-degree relatives of patients with the gene mutation associated with aneurysms and/or aortic separation (for example FBN1, TGFBR1, TGFBR2, COL3A1, ACTA2, MYH11) should receive genetic testing and prenatal counseling. Patients with this type of mutations should undergo imaging evaluation of the aorta.

b. The risk of children of the above relatives depends on whether they present the syndrome or not. In the case of a parent with MFS, the risk of having a child with this syndrome is estimated at 50%.

c. If neither of the parents have MFS then the risk is estimated at <50% (because probably a mutation in these parents may be *de novo*). This percentage is however higher than those of the general population because there are rare cases of somatic and germline mosaicism which can lead to the evolvement of MFS even without the existence of the syndrome in the parents.

d. Parents with aneurysms and/or aortic separation without the known mutation, imaging of the aorta is recommended to first degree relatives to disclose those with the asymptomatic disease. If one or more first-degree relatives have aortic dilatation, aneurysm or aortic separation then imaging of the aorta is suggested for second-degree relatives.

Pregnancy and Childbirth

Pregnant women with MFS, particularly those with an increased diameter of the root of the aorta, possess an increased risk of separation or rupture of the aorta including additional obstetric complications throughout pregnancy and more frequently during the third semester.[34-38] The risk of aortic separation or other serious complications such as endocarditis or development of heart failure has been estimated at approximately 1% in case the aortic root diameter being (ACTS) ≤40 mm.[36,37,39] This risk increases significantly for ACTS>40 mm and/or rapid increase in diameter of the aortic.[39,40] It also increases the risk of complications in pregnant women with a history of aortic dissection.[41] With relation to the above data, it might prove to be crucial to estimate the risk of separation or rupture of the aorta by

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transthoracic echocardiography (estimation of the dimensions of the aortic root and ascending aorta and the possible infection of the heart valves presence) before proceeding with childbearing. If additional imaging is required, magnetic or computed tomography is recommended.[39]

Preventive surgical intervention maybe required before attempting procreation. According to the guidelines of the European Society of Cardiology (ESC) 2011 it is recommended for ACTS ≥45 mm (or >27 mm/m²),[39,42,43] and according to the guidelines of the American College of Cardiology/American Heart Association/American Association of Thoracic Surgeons (ACC/AHA/AATS) 2010 it is recommended for ACTS exceeding 40 mm. As for pregnancies that are likely to follow it should be noted that despite the fact that successful surgical correction greatly reduces the risk of dissection of the ascending aorta, the risk to the remaining parts of the aorta persists.[36,41,43-45] During pregnancy women with MFS should be monitored clinically and sonographically even those with ACTS ≤40 mm.[35-37] This monitoring should be individualized:

1. The recommendations of the European Society of Cardiology (ESC)-2011 require ultrasound imaging every 4-8 weeks throughout gestation in patients with abdominal aortic root or the ascending aorta (ACTS >40 mm).[39]

2. The recommendations of the American College of Cardiology/American Heart Association/American Association of Thoracic Surgeons (ACC/AHA/AATS)-2010 require measuring the dimensions of the root of the aorta and the ascending aorta by means of ultrasound.[40]

3. Recommendations 2011 ESC and 2010 ACC/AHA/AATS require MRI control for pregnant women with dilation of the aortic arch, descending thoracic aorta and abdominal aorta. MRI without gadolinium administration (contrast medium) is preferred for the evaluation of the size of the aorta, although there is data (however inadequate) showing that the risk to the fetus from administration of gadolinium is low.[44]

Certainly, the imaging of the thoracic aorta requires trans esophageal scanning without the use of irradiation or administration of contrast agents.

The administration of β-blockers can be used as therapeutics because they reduce abdominal aorta and the risk of dividing the aneurysm.[39,43] It is preferable to administer either labetalol or metaprolol compared to atenolol since atenolol can negatively affect fetal growth. Also angiotensin-II blockers should not be used because they adversely affect the fetus. Constant low blood pressure should be achieved (not exceeding systolic pressure value of 130 mmHg) throughout pregnancy.[39]

In accordance with the 2011 ESC guidelines, surgery will be required in the case of a ACTS ≥50 mm rapidly evolving.[39] If ACTS >45 mm termination of pregnancy may be required followed by surgical intervention, before the embryo matures.[43]

It is generally known that women with MFS have an increased risk of complications during childbirth such as premature rupture of membranes or postpartum bleeding.[45,46] An increased risk of dissection of the aorta has also been observed after birth. Regular and careful monitoring with follow-up scans of the aorta are required in high-risk patients during the after birth period. Women with MFS who have aneurysmal dilatation of the aortic root (ACTS ≥40 mm) or a history of aortic dissection should plan their delivery in specialized Cardiothoracic Surgery Units.[39]

According to the recommendations of the European Society of Cardiology, women with a diameter of the ascending aorta <40 mm without other clinical signs have an increased risk of aneurysm rupture; a slow delivery by vaginal route is preferred, prolonged or delayed second stage combined with a Valsalva maneuver to minimize delivery exertion. Epidural anesthesia is also recommended, provided that dural ectasia is excluded by magnetic resonance imaging or computed imaging. This is a necessary step in order to avoid complications during the epidural anesthesia.[47]

Women with MFS with an ascending aorta diameter ≤45 mm, vaginal delivery is recommended, whilst women with a diameter of the ascending aorta >45 mm, a cesarean section is preferred.[39] Cesarean section is preferred for women with a high risk of complications during childbirth. In aortic dissection Type A, when the fetus is considered viable, childbirth by caesarean section is recommended, with a consequent or subsequent prompt surgical correction of this vascular lesion.

According to the guidelines in 2010 ACC/AHA/AATS for type A separation of the aorta (ascending aorta) during the first or second trimester of pregnancy urgent surgical correction and fetal monitoring are required, while during the third trimester of pregnancy delivery caesarean section and then surgical correction. For type B aortic separation or acute separation in the aortic arch, drug therapy is preferred unless surgical intervention is required for the treatment of sub-acute escape from the aorta or aortic rupture. It should be noted that hypothermia and prolonged cardiopulmonary bypass can cause fetal loss.[48]

CONCLUSION

The Marfan syndrome (MFS) is a syndrome that is inherited in an autosomal dominant manner primarily and it may be manifested by a series of events from various organs and systems. It affects one person in every 3000-5000 people in the general population. In the majority of patients it is caused by gene mutations of fimprillinis 1 [fibrillin 1 gene (FBN1)] and in some cases it was reported that such mutations are inherited as recessive manner.

MRI provides the ability to see the presence and extent

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of the aneurysm of the aorta and of these aneurysms relationship with the vessels of the aortic arch. Samples from the wall of the aortic root in tunica media can reveal fragmentation of elastic fibers, cystic necrosis, fibrosis and loss of smooth muscle fibers that reflect the damage and repair process.

Genetic testing on the mutations on the fibrillin-1 gene assists in locating the patient's affected family members and augment prenatal diagnosis. MFS final diagnosis should be based on genetic prenatal testing, medical history, clinical examination and imaging evaluation.

Before any childbearing attempt, a trans-esophageal ultrasound should be performed for the assessment of the risk in aortic separation or rupture of the aorta. Should further monitoring be required, a magnetic or computed tomography can help in the final evaluation the aorta.

A very careful detailed and regular monitoring plan with a possible immediate therapeutic intervention should be followed during gestation, since childbearing women with MFS, particularly those with an increased diameter of the root of the aorta, demonstrate an increased risk of separation or rupture of the aorta including obstetric complications notably during the third trimester:

a. During pregnancy women with MFS should be monitored clinically and sonographically exclusively those with a diameter of the root of the aorta (ACTS) ≤40 mm.

b. It is highly probable, patients with ACTS ≥40-45 mm to require preventive surgical intervention before conceiving.

c. β-blockers reduce aortic luminal dilatation and the risk of a dividing aneurysm. Metaprolol and labetalol are preferably administered, since atenolol can affect fetal development. Likewise, angiotensin-II blockers should not be used because they adversely affect the fetus. A systolic blood pressure value of no more than 130 mmHg is suggested throughout pregnancy.

d. Surgical intervention will most likely be required in an ACTS ≥50 mm.

e. Women with MFS with aneurysmal dilatation of the aortic root (ACTS ≥40 mm) or a history of aortic dissection should plan their delivery in Cardiothoracic Units.

f. Female subjects with MFS and an ascending aorta diameter ≤45 mm are advised to deliver by the vaginal route; childbearing women having an ascending aorta diameter >45 mm, caesarean section is the suggested way of giving birth.

g. Epidural anesthesia is allowed, provided that dural ectasia is excluded by MRI or computed tomography.

h. Postpartum dissection of the aorta has been observed; regular and careful monitoring should be performed weeks after delivery in high-risk patients.

AUTHORS' CONTRIBUTIONS

All authors participated in writing the paper and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any studies with human participants or animals performed by any of the authors.

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Mini Review

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Patients With Dermatomyositis/Polymyositis During Pregnancy

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ABSTRACT

Dermatomyositis (DM) and polymyositis (PM) belong to the group of inflammatory muscle diseases characterized by inflammation of the muscles. These diseases are usually studied together as dermatomyositis/polymyositis (DM/PM). Regarding pregnant patients affected with DM/PM, important individual issues arise as: (1) Do female patients with DM/PM successfully complete pregnancy, giving birth to healthy infants or is there high risk of complications for both mother and fetus? (2) Is there a connection between activity of DM/PM and high risk of complications during gestation? (3) Does pregnancy increase the risk of DM/PM activation? (4) Does pregnancy increase the risk of DM/PM relapse during or right after gestation? After our attempt to answer these questions, we will refer to the treatment of the disease during pregnancy and the effect it could have on the completion of pregnancy.

KEYWORDS: Dermatomyositis; Polymyositis; Pregnancy; CPK; Immunoglobulin; Prednisolone.

ABBREVIATIONS: DM: Dermatomyositis; PM: polymyositis; CPK: Creatinine Phosphokinase.

INTRODUCTION

Dermatomyositis (DM) and polymyositis (PM) belong to the group of inflammatory muscle diseases characterized by inflammation of the muscles and represent immune-mediated syndromes secondary to defective cellular immunity with an incidence in the United States that ranges from 0.5-8.4 cases per million population and it is more common within the black population. Evidence support the idea of a *T*-cell–mediated cytotoxic process directed against unidentified muscle antigens with the factors triggering a *T*-cell–mediated process being still unclear. Due to common symptoms and laboratory tests (increased levels of muscle enzymes), DM and PM are usually studied together. The most common symptom of those diseases is symmetric muscle weakness, pain and tenderness. DM also appears to have skin manifestations (93%) not observed in PM, a characteristic that also makes it easier to diagnose (in adittion to the other diagnostic criteria that involve abnormal elctromyograph, elevated serum levels of CK and muscle biopsy).[1-4]

Regarding pregnant patients affected with DM/PM, important individual issues arise as: (A) Do female patients with DM/PM successfully complete pregnancy, giving birth to healthy infants or is there high risk of complications for both mother and fetus? (B) Is there a connection between activity of DM/PM and high risk of complications during gestation? (C) Does pregnancy increase the risk of DM/PM activation? (D) Does pregnancy increase the risk of DM/PM relapse during or right after gestation? After our attempt to answer these questions, we will refer to the treatment of the disease during pregnancy and the effect it could have on

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the completion of pregnancy.

DERMATOMYOSITIS AND POLYMYOSITIS DURING PREGNANCY

A. Do Female Patients with DM/PM Successfully Complete Pregnancy, Giving Birth to Healthy Infants or is there High Risk of Complications for Both Mother and Fetus?

Given the international literature, a wide number of studies have focused on female patients with DM/PM where the symptoms appeared during adolescence, teenage or adult life:

1) Regarding patients contracting the disease during adolescent or teenage years.

In 1992 Pinheiro Gda et al published a case report of a woman in her 37th week of gestation with adolescent DM who due to fetal distress underwent urgent cesarean section giving birth to a healthy infant. Both the mother and the child were healthy upon reexamination eight months later.

The progress of the first gestation of a 22-year-old woman with adolescent DM was first described by Madu et al[5] while she was being treated with low dosage corticosteroids (5 mg prednisolone every two days). The examination of the fetus in 20th week of gestation was normal. An ultrasound test with Doppler analysis was conducted in 34th, 36th and 37th week showing no abnormalities. The patient presented exacerbation of skin rash on the 39th week and labor induction with intravaginal prostaglandin infusion which led to spontaneous rupture of the membranes, causing childbirth. The infant, weighting 2790 gr, and the mother were both in good condition.

2) Regarding female patients whose disease was first diagnosed with DM in adult life the conclusions are contradictory with reports advocating good pregnancy outcome, or correlation between disease activity and adverse outcome, or even initiation of the disease during pregnancy or after childbirth.[4-10]

In most cases the gestation was successfully completed with only a small number of complications. In 1984, a group of 18 women with DM/PM was studied by Gutierrez et al.[8] Ten pregnancies involving 7 women were monitored. Concerning 4 of these women the start of the gestation coincided with the beginning of the disease while with the other 3, the disease was dormant and an outbreak sometime during pregnancy occurred. Fifty-five percent of these cases ended in fetal death whilst 50% of the remaining gestation was premature terminated.

In contrast, in 1992 Ohno et al[9] presented two women with active DM who became pregnant, giving birth without complications to healthy infants.

In the study of Missumi et al[10] in 2015 regarding the progress of gestation during active DM/PM, from a total of 98 women (60 women with DM and 38 with PM) 78 pregnancies were monitored and studied between June 2011 and June 2012. The study resulted in good pregnancy outcomes (except 1 intrauterine reactivation, 1 diabetes mellitus, 1 hypertension, 1 disease reactivation, 1 hypothyroidism and 2 fetal losses) with patients developing dermatomyositis during pregnancy and 4 during the post-partum period, with good control after corticoid and immunosuppressive therapy. Therefore, the authors concluded that pregnant patients do not seem to be connected to worse prognosis or high risk for either the mother or the fetus, while the disease, either during pregnancy or the postpartum, had good outcome after therapy.

B. Is There a Connection Between Activity of DM/PM and High Risk of Complications During Gestation?

A research of the international literature proves a possible correlation between connective tissue diseases and complications during gestation. In 1998, Skomsvoll et al[11] presented a study were the births recorded in the medical birth registry of Norway in the period 1967-1995 were studied for obstetrical complications and interventions at delivery. The authors reported 72 pre-mature births, 30 pre-eclampsia cases, 42 low birth weight, reporting a possible connection between the outcomes and active disease.

Other studies also reported a more specific association between the activity of the DM/PM and the increased risk of complications during pregnancy.[12-14] However, complications of pregnancy in women whose disease was in remission were also reported[15] as well as lack of correlation between disease activity and progression of pregnancy.[8,16] Even though the results seem more satisfying than worrying, more studies need to be conducted to reach safe conclusions considering the connection of complications during pregnancy to DM/PM.

C. Does Pregnancy Increase the Risk of DM/PM Activation?

In 2014 Pinal-Fernandez et al[17] reported 102 gestations out of 51 women with inflammatory muscle disease (41 with DM and 10 with PM) diagnosed during 1983-2013. From these, 14 pregnancies regarding 8 women took place during activity of the disease. Seven women showed clinical improvement whilst exacerbation of the disease occurred in 5 pregnancies with 2 women. In other women, the disease remained inactive during pregnancy. No myopathy in any pregnancy was observed. Thus, the researchers concluded that pregnant patients with DM/PM are not accompanied by an unfavorable prognosis for the mother or the fetus, and that approximately on 50% of the patients the disease showed improvement during pregnancy.

D. Does Pregnancy Increase the Risk of DM/PM Relapse During or Right After Gestation?

The research of Missumi et al[11] in 2015 resulted in 2 patients developing the disease during pregnancy and 4 women (2 with

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DM and 2 with PM) after childbirth.

Similarly, Park et al[18] reports the appearance of a typical DM's skin rash and intense muscle weakness in the 12th week of pregnancy in a woman 22 years of age while Kofteridis et al[19] presented a patient with acute appearance of DM combined with rabdomyolysis in the 14th week of pregnancy resulting in miscarriage of the fetus. Also, Ohno et al[9] described a woman with the appearance of DM in the third trimester of pregnancy. In the second pregnancy, the possible outbreak of the DM was avoided with oral use of 0.3 mg/kg body weight prednisolone per day. Both pregnancies were successfully completed with the mother and the newborn developing no health problems.

The case of a 30 year old female that developed muscular pain and muscle weakness combined with facial, elbow and knee skin rash, while pregnant with triplets (confirmed by ultrasound) in 8th week of gestation was presented by Tojyo et al.[20] The laboratory tests revealed increased creative phosphokinase levels (CPK serum) and anti-Jo-1 antibodies. A skin biopsy showed edema in the superficial layer of the dermis and aqueous alteration in the stratum basale of the epidermis. Diagnosis of DM was then confirmed and oral treatment with 80 mg of pre-dnisolone daily without observation improved the symptoms. All the embryos died. Their death was linked to DM.

Of interest is the case of a 27-year-old woman described by Pasrija et al.[21] During the third trimester of pregnancy, the patient showed a sudden lilac rash and Gorton papules on the dorsal surface of the upper hands, weakness of the proximal muscles and palpitations combined with high creatinine phosphokinase (CPK) serum levels. Electromyography in the left deltoid muscle was conducted, showing findings compatible with myopathy while biopsy of the right deltoid muscle revealed the presence of lymphocytic inflammatory infiltrates and necrotic muscle fibers. The patient started administration of 8 mg dexamethasone intramuscularly twice daily combined with hydroxychloroquine. The muscle symptoms retreated immediately but not the skin rash. The patient experienced episodes of dyspnea and intense palpitation. In the 33rd week of pregnancy and echocardiogram revealed generalized hypokinesia on the wall of the left ventricle and 45% ejection fraction. The Doppler examination in the 36th week showed high resistance index (resistance index=0,6) in the left uterine artery. In the 37th week a healthy infant weighing 2.500 g by spontaneous vaginal delivery followed.

Relapse of DM shortly after birth or miscarriage has also been reported. In the study of Vancsa et al[12] one out of 9 patients with DM/PM, developed DM during the 3rd trimester of gestation.

In the study of Kaddour et al[14] in 9 pregnancies with an active DM/PM, an outbreak was reported in one woman 10 days after childbirth.

The Kanoh et al[22] also report the case of a female who developed DM after childbirth of a healthy infant. A similar case was described by Lee et al.[23]

The Yassaee et al[24] described in 2009 the case of a 38 year old woman that revealed cutaneous symptoms of DM 4 days after spontaneous abortion (facial erythema, Gorton papules on both hands and elbows and telangiectasias) but without muscle participation or increase of CPK levels. The skin biopsy was compatible with DM.

Treatment during Gestation

In 2015 Ochiai et al[25] reported a case of a patient with rheumatoid arthritis and interstitial pneumopathy that developed amyotrophic dermatomyositis during pregnancy, treated with pre-dnisolone that improved skin symptoms and interstitial pneumopathy as well as giving birth to a healthy infant in 35th week.

In 2007, Williams et al[26] described a case of a young first time pregnant woman where DM appeared in the first weeks of pregnancy. The administration of intravenous immunoglobulin (1 g/kg month body weight for two consecutive days) was accompanied by a decline of symptoms in conjunction with the reduction of CPK levels. The pregnancy was completed normally for both mother and fetus (healthy infant weighing 3.657, 5 g).

Likewise, in 2008 described a case of a 31-year-old woman that developed fever, muscle weakness, skin rash (periorbital and Gorton papules) as far as joint pain and CPK increase. Prednisolone was administered (60 mg/day) orally with regression of clinical events and reducing serum levels CPK. This dosage was progressively reduced to 35 mg/day. The pregnancy evolved satisfactorily but the ultrasound scan showed intrauterine growth restriction.

In the 35th week cesarean section was conducted. The infant had lower body weight (1502 g), but was in good condition. In contrast, the mother lost consciousness during spinal anesthesia and had to be intubated. The extubation was difficult because of the presence of weakness of the respiratory muscles. Intravenous immunoglobulin was administered at 20 g/day for 5 consecutive days in combination with 30 mg/day pre-dnisolone orally. The skin rash and muscle weakness subsided, the serum CPK levels decreased significantly but without full restoration of the respiratory muscles. Rehabilitation program for the respiratory muscles followed, leading to a reduction of the partial pressure of carbon dioxide ($PaCO_2$) and successful extubation attempt. The patient left the hospital in satisfactory condition only treated with low doses of pre-dnizolone.[27]

CONCLUSION

Dermatomyositis (DM) and Polymiositis (PM) are inflammatory myopathies of unknown etiology but with common symptoms. When the symptoms occur during pregnancy, the disease represents a challenge for both the patient and the obstetrician in order to follow therapy with no effect for the mother and

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especially the fetus. Most evidence support that the appropriate treatment with immunosuppressants allows a normal pregnancy without major problems and with no further risk for post-partum relapse. However, follow-up studies need to confirm such claims and to provide clear evidence on acute exacerbation during pregnancy.

AUTHORS CONTRIBUTIONS

All authors participated in writing the paper and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any studies with human participants or animals performed by any of the authors.

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Retrospective Study

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The Effect of the Introduction of Emergency Obstetric Drills on Maternal Mortality Trends in a Low-Resource Setting: A 5-Year Review at Mpilo Central Hospital, Bulawayo, Zimbabwe

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ABSTRACT

Background: Maternal deaths are very distressing to the healthcare givers and devastating to surviving family members. They decimate young, healthy women at the peak of their reproductive lives. The deaths result in orphaned children. Globally maternal deaths remain high on the agenda of the World Health Organisation (WHO) and the United Nations (UN) with the aim to reduce them. Developing nations with low/middle incomes contribute the majority of global deaths. Pregnant women in these settings face far greater risks of dying in pregnancy compared to their counterparts in rich-resourced countries. In this unit, there was an introduction of emergency obstetric drills (PROPMT®-Practical Obstetric Multi-Professional Training courses) from November 2011. These drills involved on-site training of doctors and midwives on a regular basis. This study aims to determine the effects of the introduction of such training on maternal mortality. Maternal mortality is high in the Sub-Saharan region and any reduction of the figures is welcomed.

Aims: The aims of the study are: 1) To determine the effect of the introduction of on-site emergency obstetric training on maternal mortality trends. 2) To document trends in maternal mortality in a low-resource setting. 3) To document the current maternal mortality ratio for the Mpilo Central Hospital.

Methods: This was a retrospective descriptive cohort study carried out at Mpilo Central Hospital, a tertiary teaching referral government hospital in a low-resource setting in Bulawayo, Zimbabwe. Data was obtained from the maternal mortality register of patients that had died during the period January 1, 2012 to December 31, 2016. The register contains all the demographic, clinical and outcome data. The Statistical Package for the Social Sciences (SPSS) Version 21 (IBM Corp., Armonk, NY, USA) statistical tool was used to calculate the mean and standard deviation (SD) figures. Simple statistical tests were used on absolute numbers to calculate percentages.

Results: During the period 1 January 2012 to 31 December 2016 there were 49,501 live births at Mpilo Central Hospital. There were 246 maternal deaths during that period. The mean age of the maternal deaths mothers was 29.6 years (SD±2.8) and the mean parity was 1.7 (SD±1.6). Tables 1-2 show most of the results. Maternal mortality has fallen since 2012 at the unit both in terms of direct obstetric deaths and the maternal mortality ratio (MMR) since the introduction of on-site emergency obstetric training for doctors and nurses in 2011. There was a 45.1% drop in direct obstetric deaths in the last 5 years. The MMR fell from 612 to 429 maternal deaths per 1,00,000 live births.

Conclusion: The trends in maternal mortality are that direct obstetric deaths and the MMR have been falling since 2012 in this unit, a year after the introduction of emergency obstetric drills. The current MMR for Mpilo Central Hospital is 429 maternal deaths per 1,00,000 live births. The Sustainable Development Goal of achieving an MMR of less than 70 maternal deaths per 100 000 live births by 2030 should be achieved.

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KEY WORDS: Maternal mortality; Maternal mortality ratio; Causes; Low-resource setting; Emergency obstetric drills; Mpilo Central Hospital.

ABBREVIATIONS: LSCS: Lower Segment Caesarean Section; NVD: Normal Vaginal Delivery; BID: Brought In Dead: WHO: World Health Organisation; UN: United Nations; MMR: Maternal Mortality Ratio; PROPMT®: Practical Obstetric Multi-Professional Training; HIV: Human Immunodeficiency Virus; AIDS: Aquired Immunodeficiency Syndrome.

INTRODUCTION

Maternal deaths are very distressing to the healthcare givers and very devastating to surviving family members. They decimate young, healthy women at the peak of their reproductive lives. The deaths result in orphaned children. Globally maternal deaths remain high on the agenda of the World Health Organisation (WHO) and the United Nations (UN) with the ambitious aim to reduce them. Developing nations with low/middle incomes contribute the majority of global deaths. Pregnant women in these settings face far greater risks of dying in pregnancy compared to their counterparts in rich-resourced countries.

Maternal deaths are classified as direct obstetric deaths and indirect obstetric deaths. Direct obstetric deaths are defined as those that are due the complications of pregnancy (pregnancy, labor and puerperium), from interventions, omissions, incorrect treatment or a chain of events resulting from any of these. Indirect obstetric deaths were those resulting from previous existing disease that developed during pregnancy and which was not due to direct obstetric causes, but which was worsened by the physiologic effects of pregnancy. Three-quarters of maternal deaths cases in low-resourced countries are due to direct obstetric deaths.

The UN Millenium Development Goal 5 calls for a 75% reduction in the maternal mortality ratio (MMR) between 1990-2015. The Sustainable Development Goal aims for less than 70 maternal deaths per 100 000 live births globally by 2030. Globally the MMR fell from 385 deaths per 1,00,000 live births in 1990 to 216 in 2015 corresponding to a relative decline of 43.9% with 3,03,000 maternal deaths worldwide in 2015.[1] The appropriate global lifetime risk of a maternal death fell considerably from 1:73 to 1:180 of 2015.[2] A woman in Sub-Saharan Africa has a lifetime risk of maternal death of 1 in 39 compared with around 1 in 10,000 in industrialized countries.[3] The MMR remains the highest in Sub-Saharan region at between 450-500 maternal deaths per 1,00,000 live births.[4,5]

Developing countries accounted for approximately 99% of global maternal deaths in 2015 with Sub-Saharan Africa alone accounting for roughly 66%.[2] In 2007 the MMR for Zimbabwe was 725 maternal deaths per 1,00,000 live births.[6] The MMR for this unit has not been documented before in the literature. In a similar low-resource setting in a Nigerian hospital it was found to be 645 maternal deaths per 1,00,000 live births[7] and 438 maternal deaths per 10,000 live births in a Ugandan hospital.[8]

The global causes of maternal mortality are haemorrhage, hypertensive disorders and sepsis, which account for more than half of the global deaths.[9] In Sub-Saharan region, AIDS-related deaths also contribute a significant portion and efforts to eliminate them are being done.[10]

METHODS

This was a retrospective descriptive cohort study carried out at Mpilo Central Hospital, a tertiary teaching referral government hospital in a low-resource setting in Bulawayo, Zimbabwe. The PROMPT® involved regular on-site training for doctors and midwives 3 or 4 times. It also involved placing clearly labelled and regularly stocked boxes in the labour ward. These boxes were for the common obstetric emergencies like postpartum hemorrhage (PPH). The Ethics Committee at Mpilo Central Hospital gave a waiver for retrospective and non-intervention studies to go ahead in the institution as long as the data remained anonymous. No ethical issues arose during the study as all the data were anonymous. No patient consent was necessary. Minutes of the Committee's inaugural meeting held on the 13th October 2016 set out the requirements of all the studies at the institution.

Data was obtained from the maternal mortality register of patients that had died in the period January 1, 2012 to December 31, 2016. The register contains all the demographic, clinical and outcome data. The Statistical Package for the Social Sciences (SPSS) Version 21 (IBM Corp., Armonk, NY, USA) statistical tool was used to calculate the mean and standard deviation (SD) figures. Simple statistical tests were used on absolute numbers to calculate percentages.

RESULTS

During the period 1 January 2012 to 31 December 2016 there were 49,501 live births at Mpilo Central Hospital. There were 246 maternal deaths during that period. The mean age of the maternal deaths mothers was 29.6 years (SD±2.8) and the mean parity was 1.7 (SD±1.6). Tables 1-2 show most of the results.

Maternal mortality has fallen since 2012 at the unit both in terms of direct obstetric deaths and the MMR. There were 60 maternal deaths recorded in 2012 and 39 maternal deaths by 2016. There was a 45.1% reduction in direct obstetric death figures. The MMR fell from 612 to 429 maternal deaths per 1,00,000 live births.

Direct obstetric deaths constituted 80.5% of the total maternal deaths, indirect obstetric deaths 17.5% and 2.0% were of unknown causes. The direct maternal deaths fell to 71.8% at

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Table 1: Trends in Maternal Mortality.

Year	Live births	Maternal deaths	MMR/100000 live births
2012	9800	60	612
2013	11198	52	464
2014	10411	50	480
2015	9008	45	500
2016	9084	39	429
Totals	49501	246	497

Table 2: Trends in Direct and Indirect Obstetric Deaths.

Year	Maternal deaths	Direct obstetric deaths	Indirect obstetric deaths	Unknown
2012	60	51 (85.0%)	8 (15%)	0
2013	52	42 (80.8%)	9 (17.3%)	1 (1.9%)
2013	50	43 (86.0%)	6 (14.0%)	0
2015	45	34 (75.6%)	10 (22.2%)	3 (6.7%)
2016	39	28 (71.8%)	10 (25.6%)	1 (2.6%)
Totals	246	198 (80.5%)	43 (17.5%)	5 (2.0%)

the end of the study.

DISCUSSION

Maternal mortality trends showed encouraging statistics. There has been a 45.1% reduction in direct obstetric deaths since the introduction of on-site emergency training for doctors and nurses in the unit. There has been a sustained fall in the MMR since 2012 from the high of 612 maternal deaths per 1,00,000 live births to 429 maternal deaths per 1,00,000 live births by 2016. This is a reduction of 29.9%. The current MMR is slightly similar to figures from a similar hospital in Nigeria (465) and Uganda (438). The current MMR for the unit is below the 450-500 maternal deaths per 1,00,000 live births recorded for the Sub-Saharan Africa region. The falling trends in maternal mortality are in keeping with the recorded fall in global maternal death figures.

The introduction of regular obstetric drills,[11,12] is associated with quality improvements. Regular audits and accountability[13] for each and every poor perinatal outcome may also help improve outcomes. Routinely collected obstetric data could help in monitoring and guide quality improvement.[14,15]

Priorities in reducing the mortality burden are provision of safe caesarean section, prevention of sepsis and appropriate care of women in labour.[16] The association between unbooked mothers and poor outcomes was found in this study with 76% of maternal deaths being unbooked. Antenatal care should be a universal norm for all pregnant women if we are to tackle the problems of global maternal deaths.

CONCLUSION

The trends in maternal mortality show that direct obstetric deaths and MMR have been falling since the introduction of on-site emergency obstetric training. This is in keeping with global trends in maternal mortality. Direct obstetric deaths fell by 45.1%. The current MMR for Mpilo Central Hospital is 429 maternal deaths per 1,00,000 live births, similar to figures reported in the literature of similar hospital in low-resource settings.

More efforts should be applied to reduce these maternal death figures further. The goal of achieving an MMR of less than 70 maternal deaths per 1,00,000 live births by 2030 should be achieved. The provision of universal antenatal care with accessible and affordable healthcare facilities would go a long ways in helping pregnant women fulfill their reproductive rights without having to die to achieve this right. Young pregnant women are still dying of preventable direct obstetric causes that are largely preventable as seen in rich-resourced countries.

DECLARATIONS

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