

Effects of pregnancy hormones on burn wound healing: A prospective study**Manohar K. Malviya¹, Sameer Soni^{2*}, Devendra Dhakad³, Anjali Mittal⁴**¹*Assistant Professor, Department of Surgery, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India*²*Assistant Professor, Department of Surgery, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India*³*Assistant Professor, Department of Surgery, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India*⁴*Junior Resident, Department of Surgery, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India***Received: 11-06-2021 / Revised: 16-08-2021 / Accepted: 16-09-2021****Abstract**

Objective: The incidence of female thermal burn patients of reproductive age varies from 0.6%-15% in different series with the highest incidence reported from India. With improvements in the general survival of burns patients, the pregnant woman with burns also stands a better chance of survival today. **Patients and methods:** This is an observational study. The study was carried out during the period from January 2018 to March 2021, at the Department of Surgery, Chirayu Medical College and Hospital, Bhopal. The total number of pregnant female patients were 10, and non-pregnant female patients were 40, aged between 19-40 years and depth of burn was greater than the first-degree burn. The study was done on the basis of age, the percentage of body surface area of burn, pregnancy vs non-pregnancy, wound healing, average length of hospital stay. **Results:** There were 10 pregnant and 40 non-pregnant burn female patients; assessed after initial burn resuscitation period with stable vitals. The mode of injury was predominantly domestic fire. The percentage of TBSA varied from 1% to 40%. It was found that the average length of stay in the hospital was less for pregnant females than the non pregnant females. Average length of hospital stay for pregnant females with burns was 9 days. Average length of hospital stay for non pregnant females with burn was 13.5 days. **Conclusion:** Burn wounds in pregnancy are associated with better and rapid healing due to the effects of pregnancy hormones. Circulating blood volume is also high in the pregnant patients which are associated with good tissue perfusion and better wound healing.

Keywords: Pregnancy, wound healing, burn.**Key message:** In pregnant females burn wound healing is rapid and well in comparison to non-pregnant burn females due to the effect of pregnancy hormones on wound healing.

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Introduction

The incidence of female burn patients of reproductive age varies from 0.6%-15% in different series with the highest incidence reported from India [1-6]. Thermal injuries usually occur at home and are caused by flame burns or hot liquid scalds. The interest of the foetus must also be borne in mind constantly throughout any course of treatment. With improvements in the general survival of burn patients, the pregnant woman with burn also stands a better chance of survival today. The treatment is especially difficult since the clinician has to treat both the mother and the foetus each with different medical needs.

Patients and methods

This is an observational study. The study was carried out during the period from January 2018 to March 2021, at the Department of Surgery, Chirayu Medical College and Hospital, Bhopal.

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Pregnant and non-pregnant females with thermal burn admitted to the hospital during the period were included in the study. Patients were assessed after initial burn resuscitation period (until the patient has stable vitals). The injuries were predominantly domestic fire. The study was done on the basis of age, the percentage of burn (total body surface area), pregnancy vs non-pregnancy, wound healing.

All patients received routine thermal burn care, including fluid, wound care with a wound dressing, antibiotics as per wound swab culture and sensitivity test and nutritional support. State of the foetus was recorded at admission and monitored clinically as well as with weekly USG and the rate of wound healing, vitals and general conditions of patients were assessed. Comparison of wound healing was done only in those patients who have survived for more than 2 weeks from day of burn injury.

Inclusion Criteria

- Patients with age between 18 years to 40 years (pregnant and non pregnant females).
- Females with depth of burn greater than the first degree burns.
- Females with burns up to 40% TBSA.

Exclusion Criteria

- Non pregnant females with any co morbidities like type 2 diabetes mellites, hypertension etc.
- Pregnant females with complicated pregnancy like gestational diabetes mellites, eclampsia etc.
- Immunocompromised subjects.

Results

The average length of hospital stay for pregnant females with TBSA of burn 1-20% was 8 days. While the average length of hospital stay for pregnant females with TBSA of burn 21-40% was 10 days. (Table 1) The average length of hospital stay for non pregnant females with TBSA of burn 1-20% was 12 days. While the average length of

hospital stay for non pregnant females with TBSA of burn 21-40% was 15 days. (Table 2)

Average length of hospital stay for pregnant females with burns was 9 days.

Average length of hospital stay for non pregnant females with burn was 13.5 days.

Table 1: Pregnant females: No. of days of hospital stay

% of TBSA of burn	Total no. Of pregnant burn patients	No. of days of hospital stay
1% - 20%	3	8
21%-40%	7	10
Total	10	18

(TBSA: Total Body Surface Area)

Table 2: Non-pregnant females: No. of days of hospital stay

% of TBSA of burn	Total no. of non-pregnant burn patients	No. of days of hospital stay
1% - 20%	25	12
21%-40%	15	15
Total	40	27

(TBSA: Total Body Surface Area)

Discussion

During pregnancy cardiac output doubles with resulting increase in peripheral blood flow. With this increased blood flow to the mother's tissues, wound healing may well be enhanced. Heartbeat and blood volume during pregnancy- During the second trimester of pregnancy, the mother's heart at rest is working 40% harder. Most of this increase results from a more efficiently performing heart, which ejects more blood at each beat. Heart rate may increase up to 15% during pregnancy. Blood volume increases progressively during pregnancy, beginning from 6-8 weeks and continuing until weeks 32-34. The volume of plasma increases 40-50% and red blood cell mass 20-30%, creating a need for increased iron and folic acid intake.

Respiratory and metabolic changes

Because of increased demand for blood and the dilation of blood vessels, pregnant women experience increase in the amount of oxygen they transport in their blood. This growth also forces an increase in metabolic rates during pregnancy, requiring women to up energy intake.

Breathing and blood Oxygen Levels

During pregnancy, the amount of air moved in and out of the lungs increases by nearly 50% due to two factors. Each breath has a greater volume of air, and the rate of breathing increases slightly. Overall, pregnant women have higher blood oxygen levels. Studies have shown that pregnant women consume 10 to 20% more oxygen at rest. Metabolic rate is also increased during pregnancy.

Specific hormonal levels are increased during pregnancy, which may affect the wound healing and maintains the pregnancy.

These hormones are as follows

Human chorionic gonadotrophin (HCG) - plays a key role in: -

1. Angiogenesis by inducing vascular endothelial growth factor (VEGF) up-regulation[7,8].
2. Tissue remodelling by increasing matrix metalloproteinase-9 production, Zygmunt et al[9]. Showed that hCG was able to promote angiogenesis by stimulating EC (endothelial cells) migration and capillary sprout formation.

Human Growth Hormones

During normal pregnancy, there is a progressive increase in maternal serum GH[10] and insulin-like growth factor-I (IGF-I), intrauterine growth retardation has been associated with low circulating maternal IGF-I and low placental GH concentrations[11]. HGH increases the influx of amino acids into the cell and decreases the efflux. Cell proliferation is accentuated as is overall protein synthesis and new

tissue growth. HGH also stimulates IGF-1 production by the liver, and some of the anabolism seen with HGH is that produced by IGF-1, another anabolic agent[12,13]. Clinical studies have in large part focused on the systemic anabolic and anticatabolic actions of HGH[14,15]. Populations, where HGH has been shown to be beneficial, include those with severe burn and trauma, those with HIV infection with wasting, and the frail elderly. Other effects on the wound include increased rate of re-epithelialization of skin graft donor sites in adults and children with severe burns or trauma[16,17]. HGH has been shown to increase wound collagen content, granulation tissue and wound tensile strength and the local production of IGF-1 by fibroblasts.

Oestrogens

Levels of estrogen are high in a woman's body during pregnancy, the levels fall dramatically after childbirth. In normal unwounded skin, topical estrogen treatment to some degree reverses 3 age-related skin conditions: 1) skin atrophy by stimulating keratinocyte proliferation and reducing apoptosis, increasing dermal collagen production, and inhibiting MMP expression; 2) skin dryness by altering keratinocyte function, increasing dermal water holding capacity, and increasing sebum production; and 3) skin wrinkles by increasing dermal water holding capacity and increasing number and improving orientation of elastin fibers[18]. Systemic HRT significantly accelerates acute wound healing in the elderly, and topical estrogen treatment accelerates the rate of healing in men and women[19,20]. Estrogen affects macrophages by reducing production of a range of pro-inflammatory cytokines, including interleukin 6 (IL6)[21], tumor necrosis factor- α (TNF- α), and macrophage migration inhibitory factor (MIF)[22]. Estrogen is mitogenic for keratinocytes, accelerating re-epithelialization and fibroblasts, increasing synthesis of numerous extracellular matrix components, particularly collagen. In a recent case-cohort study, Margolis et al[23] identified reduced risk of developing venous leg or pressure ulcers in elderly women undergoing HRT. Estrogens enhance the humoral immune response [24]. Ashcroft and colleagues provided the first cogent evidence that estrogens enhance the repair of damaged skin[25].

Progesterone- Progesterone is produced in a woman's ovaries and in the placenta of a pregnant woman. Progesterone also has a role in skin elasticity and bone strength. Progesterone raises epidermal growth factor-1 (EGF-1) levels, a factor often used to induce proliferation and used to sustain cultures, of stem cells. Progesterone acts as an anti-inflammatory agent and regulates the immune response. Progesterone normalizes blood clotting and vascular tone, zinc and copper levels, celoxigen levels, and use of fat stores for energy.

Oxytocin

The pituitary gland secretes this hormone in the brain. The hormone can improve the wound healing process. Along with being a pain reliever, the neurotransmitter activates the immune system's regulatory cells, helping defend against infection and, in effect promoting faster, more efficient recovery.

Thyroxin

Thyroid enlargement with a 20 % increase in function (from tissue hyperplasia and increased vascularity) occurs in pregnancy. Thyroid hormone accelerates barrier formation by increasing the activity of enzymes in the cholesterol sulphate cycle, and hypothyroidism may hinder the epidermal barrier function[26,27]. In tissue culture studies, T3 has been shown to directly stimulate proliferation of both epidermal keratinocytes and dermal fibroblasts[28-30]. T3 is necessary for the keratinocyte proliferation required for optimal wound healing. T3 exerts influence by stimulating expression of the proliferation cytokeratins 6a, 16, and 17. Lennox and Johnston[31] reported that exogenous T4 improved the rate of wound healing in rats as well as the strength of the scars. Some authors report improved rates and quality of wound healing in response to TH[32-37].

Insulin

The hormone insulin is known to have anabolic activities in addition to its effect on glucose and fat metabolism[38]. An increase in circulating amino acids produced by wound amino acid intake increases the anabolic and anticatabolic effect in both normal humans and populations in a catabolic state[39-41,42]. A number of clinical trials, mainly in burn patients have demonstrated the stimulation of protein synthesis and decreased protein degradation and net nitrogen uptake, especially in skeletal muscle[42,43]. Serum insulin levels were significantly higher in 3rd trimester when compared with 2nd trimester and those of the 2nd trimester were significantly higher when compared with 1st trimester.

Prolactin

Is a potent immunomodulator capable of undertaking a specific role in regulating the immune response both humoral and cell-mediated one. It is believed that PRL expression in the skin can probably be related to an inflammatory response and may play a role in the wound healing process. During pregnancy, high circulating concentrations of estrogen and progesterone increase prolactin levels by 10- to 20-fold. Estrogen and progesterone inhibit the stimulatory effects of prolactin on milk production. The abrupt drop in estrogen and progesterone levels following delivery allows prolactin which temporarily remains high to induce lactation. It seems that VEGF is also produced by macrophages stimulated by PRL[45,46]. It is believed that PRL expression in the skin can probably be related to an inflammatory response and may play a role in wound healing[44,47,48]. PRL-receptor (PRL-R) is widely expressed in several and distinct tissues and it was identified in human skin too[49,50]. Several recent studies suggest that PRL contributes to a wide variety of cutaneous processes, both physiological and pathological[44]. In wound healing that requires appropriate responses by fibroblasts and endothelial cells; it was shown that these cells express PRL-R [44,51], so the cutaneous vascular system could provide new important details in relation to PRL-induction on angiogenesis. The presence of PRL-R on endothelial cells also suggests a direct action of PRL on angiogenesis, in addition to that mediated by growth factors such as VEGF. Various studies have suggested that all above-mentioned hormones take participation in wound healing. If these hormones levels are high in the body, it promotes the wound healing and if its levels are decreased, it delays the healing. In pregnancy, all above-mentioned hormone levels are increased as mentioned in various studies and assist in maintaining the pregnancy. These increased circulating hormones also promote the wound healing. Pregnancy associated hormone levels are decreased after delivery or abortion. In this study, we have observed that fetus abortion or delivery adversely delays the wound healing.

Those pregnant females who couldn't maintain their pregnancy or aborted due to burn stress or due to any other reasons, the wound

healing in these patients was very slow and also the wound healing was delayed.

Conclusion

In pregnant females wound healing is better and rapid in comparison to non-pregnant burn females due to the effect of pregnancy hormones on wound healing. Circulating blood volume is also high in the pregnant patients so it provides good tissue circulation and rapid wound healing. Pregnancy is protective in burn patients by improving the healing of wound after initial burn management.

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