

## **PORCINE BASED ANTICOAGULANT IN PREGNANCY REVISITED: ANALYSIS AND DISCUSSION OF NATIONAL FATWA IN ALIGNED WITH ISTIHALAH FIQH CONCEPT IN CLINICAL PRACTICE**

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### **ABSTRACT**

*Recent studies around the world have shown that there is an increment of maternal mortality due to the rising incidence of blood clot complication or commonly known as venous thromboembolism in pregnancies and during confinement. Women with high risk pregnancies are treated with low molecular weight heparin (LMWH) as the effective anti coagulant either during antenatal period or post delivery depending on their risk for certain duration. Thus, has shown to improve and reduce the maternal mortality and morbidity rate. Unfortunately, the usage of LMWH which are porcine in origin has raised a concern among Muslim health practitioner and public, although it is clinically proven to be the safest anti-coagulant treatment for pregnant women with complications following venous thromboembolism event. This article was meant to analyse the fiqh concept of istihalah between scholars and evidence, regarding the usage of porcine based LMWH among pregnant women. Fiqh method upon istihalah, references and content analysis; supported with more recent clinical evidences were analysed and elaborated regarding this issue and its clinical usage of LMWH upon pregnant mothers. There were unduly debate between Muslim scholars and Muslim health practitioners around the globe regarding the usage of porcine base LMWH as the best treatment in preventing and treating venous thromboembolism using LMWH. The istihalah concept has allowed many Muslim scholars in other countries to agree on the usage of LMWH in clinical practice. Nevertheless, Malaysian National Fatwa council has issued to forbid the usage of LMWH due to availability of other anticoagulant options. Yet; new evidences in which absent of porcine traces after manufacturing of LMWH proven safety profile of porcine base anticoagulant has emerged and has change the perspectives of clinical practice. These arguments hopefully able to facilitate the justification of istihalah concept in permissibility of LMWH usage in clinical practice among Muslim health practitioner and create public awareness.*

Keywords: *Maternal, pregnancies, istihalah, low molecular weight heparin, fiqh.*

## INTRODUCTION

The global maternal mortality rate has decreased tremendously over the last few decades as the advance development of medical technologies and improvement of health care services worldwide. The systematic health care programmes for pregnant mothers as well as increasing numbers of well equipped facilities and trained medical personnel along with health care providers have contributed to almost 50% dropped in the figures for maternal mortality. However, the numbers seems static until the year 2015 (Department of Statistic Malaysia, 2017).

Many efforts have been done to further decrease these figures as maternal mortality is one of the important components in the targeted 5<sup>th</sup> “*Malaysia Millenium Development Goal*”. This is a very crucial parameter for a country’s development whereby the development are measured by the “*United Nations*” (UN) from the ability to provide good health care system primarily the pregnant mothers and sustained good maternal and fetal outcome (United Nation Malaysia, 2015).

Although post partum haemorrhage was the number one killer for pregnant mothers in labour especially in the developing country, the figures seems decreasing and static. Yet, the current trend of obstetric thrombo-embolism seems to be on the rise. These thrombo-embolism events commonly occur in the lung (pulmonary embolism) and along the veins over the lower limbs (deep vein thrombosis) which very much pregnancy related. In United Kingdom, 89 percent of maternal death contributed by this condition between the year 2003-2005. Fortunately, the percentage dropped to 70 percent lower as soon as guidelines in managing the case were introduced, followed by intensive efforts in treating it using the anticoagulant drug therapy (Centre for Maternal and Child Enquiries (CMACE), 2011). Malaysia was among the country that had been using this anticoagulant therapy as treatment of this condition.

Generally, all pregnant women have a higher coagulable blood and almost stagnant blood flow in their body. This is very much contributed by the physiological changes of the pregnancy itself to accommodate the nutrition to the growing baby and to avoid the mother to bleed to death upon delivery. This normal physiological changes further thickened blood flow with presence of other few risk factors such as advance maternal age upon approaching the pregnancy, smoking, obesity and many other risk factors which are contributed by medical back ground and lifestyle (RCOG United Kingdom, 2015). Despite known risk factor, the early symptoms might not easily detected as pregnancy symptoms may mask the presentation such as feeling fatigue, shortness of breath and swollen legs. Thus screening of risk factors early in the pregnancy and early treatment is crucial and the main principle of the treatment. The current treatment is by using the low molecular weight heparin (LMWH) as anticoagulant to help in thinning the blood flow and diluting the clots among these pregnant mothers (RCOG UK, 2015 & MOH Malaysia 2013).

This article was written to further debate and discusses the usage of LMWH anticoagulant treatment in relation to the ‘*istihalah*’ concept in Islamic *fiqh* jurisprudence. The discussion will be divided into two parts; the first part of discussion will include medical and health view and opinion in the usage of LMWH anticoagulant treatment. The

second part will be the discussion regarding the 'istihalah' concept using the LMWH as treatment among Muslims patients and the application to our daily living.

## THE USAGE OF LOW MOLECULAR WEIGHT HEPARIN IN OBSTETRIC MEDICINE

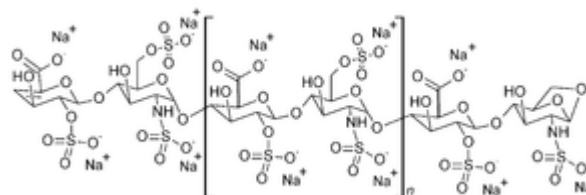
Various studies have been done upon the efficacy and safety profile upon pregnant mothers using LMWH as anticoagulant either as prophylactic or treatment dosage. These studies did review on many perspectives of the anticoagulant including the safety profile, embryopathy effect, feasibility, efficacy, potency, side effect and complication to both mother and baby. Not to mention the cost effectiveness of the medication and comparable to other types of anticoagulant. There were many types of anti coagulant drug available in the current market with wide range of price, availability, and efficacy and safety profile; yet, the usage in pregnancy and risk to the unborn child is the main concern. Furthermore, a pregnant woman undergone a lot of physiological changes to their physical, physiological and biochemical profile to the extent the bioavailability, and metabolism of drug may affect differently. Thus, this topic aimed to discuss in depth regarding the current anticoagulant specifically the LMWH treatment used among pregnant women.

Low molecular weight heparin (LMWH) is one of the common anticoagulant drugs used as blood thinning drug. It is called as low molecular weight heparin as the molecules were in smaller size as compared to the conventional unfractionated heparin drug. In Malaysia, there are two types of LMWH that is available for medical preparation, Enoxaparin Sodium (Clexane) and Tinzapain (Innohep) which are individually packed in a specialized syringe. These medications are used to be delivered under the subcutaneous layer of the skin by injecting with a needle. The usage of LMWH as blood thinning agent are highly recommended as compare to conventional usage of *unfractionated heparin* due to better safety and stable pharmacokinetic profile. Thus less risk and complication to patients' especially pregnant mother (Ian A. G& Catherine NP, 2005).

### Pharmacokinetic of Low Molecular Weight Heparin (LMWH)

Low molecular weight heparin (LMWH) is produced from chemical depolymerization using enzymes from the mucosa layer of the porcine small bowel. The chemical structure has higher anti-thrombotic and anti-coagulant properties as compared to unfractionated heparin. It binds to anti-thrombin II in cellular level where it inhibits the coagulation cascade activity; specifically clotting factor IIa and Xa. Thus, leading to thinning of blood by less aggregation of the platelets (Garcia DA, Baglin TP, Weitz JJ&Samama MM, 2012). This activity triggered at the specific dosage given calculated according to patient's body weight. It is the safest anticoagulant in pregnancy due to its property and individual dose specific preparation (Sanofi.co.uk, 2011)

Figure 1: Chemical Structure OnLMWH(Enoxaparin)



### **Clinical Application of Low Molecular Weight Heparin (LMWH)**

Anticoagulant has been used for various treatment of clotting disorders or even complication following blood clotting problems such as ischaemic heart disease or cerebrovascular accidents. Our discussion is more towards the usage in pregnancy and post partum period. Pregnant women are at higher risk of blood clotting problems as compared to normal population as the physiological changes in pregnancy itself causing them to become hypercoagulable. Thus, these young women at reproductive age are far more at risk to develop clotting problems which includes, pulmonary embolisms, ischaemic heart attack, cerebrovascular accidents, recurrent miscarriages, fetal growth restrictions and even death of the mother and unborn child.

Although pregnancy is a risk by itself, only some group of women will require treatment with anticoagulant. The obstetricians will need to assess these women and risk stratified them during their booking in first trimester to determine their requirement, indication and even calculated dosage. This is because, studies have shown there are women who are at higher risk of developing venous thromboembolism problems as compare to other pregnant women which include, previous history of thromboembolism, obesity, high parity and advanced maternal age. These women in the high risk group are predisposed to higher risk of mortality and morbidity to both mother and baby (RCOG UK, 2015 & MOH, Malaysia, 2013).

The usage of LMWH are divided into two groups, prophylaxis treatment whereby the medication is used to prevent further complication of thromboembolism. Secondly, as the treatment dosage whereby the higher dose is given to treat a hypercoagulable state of the patient or to help to de-clogged the thrombosis itself. This is because the prophylaxis dose are lower than treatment dose, and it also depends on patient weight to reach treatment level. The duration of treatment also varies depending on prophylaxis or treatment dose and the risk factors involved. Definitely, detail assessment regarding the dosage and duration will be determined by the obstetrician base on written guidelines (RCOG UK, 2015) (MOH, Malaysia, 2013).

Patient with high risk factors such as certain inherited haematological or autoimmune disorders that are high risk to develop thrombosis events especially in pregnancy, they will require certain prophylaxis dosage prior to embarking into the pregnancy accompany with close monitoring and counselling from the medical experts in preconception assessment. Same goes to women whom had cardiac valve replacement and on lifelong anticoagulant, the pregnancy should be planned and type of anticoagulant will be converted to LMWH due to better safety profile and risk of fetal anomaly on warfarin. As matter a fact, pregnancy is like a death sentence for them if it is not properly planned. The anticoagulant should be covered and adjusted to achieve safe motherhood, lower risk to the mother and baby. A successful pregnancy and healthy mother and baby are achievable with lower risk for complications using specifically tailored medication with LMWH (RCOG UK, 2015).

Yet, some women need the LMWH treatment only for certain short duration due to their background profile such as obesity, age more than 35 year old, smoking, prematurity, twin pregnancy and post operative delivery. Similarly to women whom previously had history of thrombosis, such as stroke (cerebrovascular events) or pulmonary embolism. The list of risk factors are listed according to studies and protocols made by the consensus among the medical and obstetric experts, Royal College Of Obstetric And Gynaecology, United Kingdom in 2015 (RCOG UK, 2015).

The protocol has a complete list of women with high risk medical profile requiring the LMWH treatment either as prophylaxis or as treatment dosage. It also stated the duration, type of best anticoagulant available and close monitoring required from antenatal to post natal period. These women will be divided into high risk, intermediate and low risk groups (RCOG United Kingdom, 2015& MOH, Malaysia, 2013). Otherwise, most women require the anti coagulant treatment only for short duration during post delivery due to the low risk assessment up to ten day post partum. These women are the ones in the low risk group such as delivery via caesarean section or due to age and high body mass index (RCOG UK, 2015&MOH, Malaysia, 2013).

There were many studies were done regarding the safety profile of all anticoagulant including LMWH in pregnancy, including the effectiveness and efficacy of preventing pulmonary embolism and deep vein thrombosis, recurrent miscarriages, intrauterine growth restricted babies and risk of intra-uterine death. Systematic reviews revealed that the LMWH had the best safety profile throughout pregnancy, in preventing the above incidents from the unfractionated heparin. Furthermore, it has fewer complications to the patients with lower risk for maternal mortality and morbidity, with higher successful live births (Ian A.G & Catherine N.P, 2005 &RCOG UK,2015).

#### **THE ISTIHALAH CONCEPT IN FIQH**

The word *istihalah* originates from the Arabic word of *ha-wa-la* which means 'change'. Among the fiqh scholars, the discussion regarding *istihalah* are referred to the changes that occurs to the unclean and non-purified substance into a purified form (*al-Fayyumiyy*, N.d). Within this discussion, there are few other common Arabic words that is related to the discussion of *istihalah* among the previous Islamic scholars which include "*istihlak*" and "*inqilab al-ʿayn*" (Saadan Man, 2014).

According to one of the famous fiqh scholar in Shafi'iyy'smadhhab, IbnHajar al-Haytamiyy (2001), *istihalah*is changes that occurs to the physical structure or the physical condition only, yet there is no changes in '*dhat*'. Dr. Wahbah al-Zuhayliyy (1997) in his book, "*al-Fiqh al-IslamiyywaAdillatuhu*" had elaborated that *istihalah* is actually the process of the original '*dhat*' or a being from the '*najis*' or unclean into a new purified '*dhat*' or presence. He also refers the uncleaned form of something which is bound to be '*haram*' becoming something that is permissible in Islam due to the changes that it has undergone.

However, according to IbnʿAbidin (1996), the changes or transformation of *istihalah* processcan occur in two conditions, whether it was fully transformed in total (*kulliyy*) or only some parts of the physical changes had occurred (*juz'iyy*). A simple example is that, in processing olive smeared with '*najis*' to make soap and the process of alcohol turning into vinegar over time; both either naturally happened or through a specific synthetic process.

Associate Prof. Dr.Anisah Ab. Ghani (2014) in her article entitle "*KonsepIstihalahdanHubungannyaDalamPenentuanHukumMakanan*", discussed regarding *istihalah*'s theory in depth as she explained that it is a mixture between the unclean substance or known as '*najis*' with a purified and clean substance which leads to changes in the '*dhat*' of the unclean substance becoming purified or both of these substance had mixed and inseparable.

While, Prof. Dato' PadukaDr.MahmoodZuhdiHj. Ab. Majid has given his theory which was similar as the theory of digestion system in the body. The digestion system is known to be able to breakdown and process any food or substance from its original form

and the final end product produce is totally different from its original form. During the *istihalah* process, there are many mechanical and non mechanical involve which occurs in stepwise processes before the final form of the substance is produced. A simple example in mechanical process is the process of transforming a dirty waste water becoming a totally purified water which is clean, yet suitable to drink. The process involved in transforming the clean purified water from the dirty waste is called *istihalah*. In another hand, *istihalah* in a non mechanical example is when a gambling money is given to the 'baitulmal' which this money will be later used and divides to the poor and needy (NorhidayahPuzi&Saadan Man, 2015).

## Overview Among Madhhab Upon Istihalah

### Shafi'iy Madhhab

According to imam al-Shiraziyy (N.d) in his book "*al-Muhadhdhab fi Fiqh al-Imam al-Shafi'iy*":

ولا يطهر شيء من النجاسة بالاستحالة إلا شيئين: أحدهما جلد الميتة إذا دبغ وقد دللنا عليه في موضعه والثاني الخمر إذا استحالت بنفسها خللاً فتطهر بذلك

Which means, "Something that have been know impurity will not be purified by *istihalah*, unless in two things: (one): the skin of the dead animals if it is cleaned (*samak*), and we have shown it in its place. (second): an alcohol if it was changed (*istihalah*) by itself into vinegar, it's considered pure".

While Ibn al-Naqib al-Shafi'iy (1982) written in his kitab "*Umdat al-Salik wa Uddat al-Nasik*" did mention:

ولا يطهر شيء من النجاسات، إلا الخمر إذا تخلل، والجلد إذا دبغ، ونجساً يصير حيواناً. فإذا تخللت الخمر بغير إلقاء شيء فيها - إما بنفسها أو بنقلها من الشمس إلى الظل وعكسه أو بفتح رأسها - طهرت مع أجزاء الدن الملاقية لها، وما فوقها مما أصابته عند الغليان، وإن ألقى فيها شيء فلا

Which means, "And it does not purify anything from filth (unclean), except liquor that turns into vinegar, and tanned (*samak*) skin, and something that turns into insect (such as the worm produced from the stool). If the changed of liquor without mixing anything on it -either by itself or changed the position from under the sun to shady place and vice versa or open the cap- It is still considered purify, but if it was thrown something into it (like gravel), then it is not pure".

### Hanafiyy Madhhab

Imam al-Zayla'iy (1984) in his kitab "*Tabyin al-Haqa'iq Sharh Kanz al-Daqa'iq wa Hashiyat al-Shalbiyy*";

وَكُلُّ مَا لَا يَنْعَصِرُ بِالْعَصْرِ وَالْأَعْيَانُ النَّجِسَةُ تَطْهُرُ بِالِاسْتِحَالَةِ عِنْدَنَا وَذَلِكَ مِثْلُ الْمَيْتَةِ إِذَا وَقَعَتْ فِي الْمَمْلُوحَةِ فَاسْتَحَلَّتْ حَتَّى صَارَتْ مِلْحًا وَالْعَذْرَةَ إِذَا صَارَتْ تُرَابًا أَوْ أُحْرِقَتْ بِالنَّارِ وَصَارَتْ رَمَادًا فَهِيَ نَظِيرُ الْخَمْرِ إِذَا تَحَلَّلَتْ أَوْ جِلْدَ الْمَيْتَةِ إِذَا دُبِعَتْ فَإِنَّهُ يُحْكَمُ بِطَهَارَتِهَا لِإِسْتِحَالَةِ وَذَكَرَ فِي الْفَتَاوَى أَنَّ رَأْسَ الشَّاةِ لَوْ أُحْرِقَ حَتَّى زَالَ الدَّمُ يُحْكَمُ بِطَهَارَتِهِ، وَكَذَا الْبِلَّةُ النَّجِسَةُ فِي التَّنُورِ تَزُولُ بِالْإِحْرَاقِ

Which means, “An unclean thing will be purified by istihalah, as an example, the dead animal becoming a carcass on a salt pile until it is united with salt, and the animal stools that turn into soil or burn with fire to ashes. This condition is similar to the liquor that turns into vinegar or animal skins that are purified by the samak process due to its change (istihalah). It also mentioned in al-Fatawa that the blood on the head of goat when it is burned, it becomes purify. As well as the filth soil, if we made pottery using that soil then burned it on fire, then it considered purified”.

While al-Imam MullaKhisro (N.d) in his kitab named “Durar al-Hukam Sharh Ghurar al-Ahkam” mentioned:

فَإِنَّ الْأَعْيَانَ تَطْهَرُ بِالِاسْتِحَالَةِ كَالْمَيْتَةِ إِذَا صَارَتْ مِلْحًا، وَالْعَذِرَةَ إِذَا صَارَتْ تُرَابًا، وَالْحَمْرَ خَلًّا وَنَحْوَ ذَلِكَ

Which means, “The objects are purified with istihalah, like a carcass in the salt field (then its dissolved into salts), such as stool (shit) become soil, liquor into vinegar, then it was no longer claimed as a filth/impurified”.

According to Ibn Nujaym (1968) discussion in his book, “al-Bahr al-Ra’iq”, his view upon the issue of istihalah; istihalah is a process when something or a substance in its original form is considered as ‘*najis*’ or the unclean where there after undergone changes in its component becoming a pure ‘*dhat*’ in its substance. Similar example been given in the process where an alcoholic beverage undergone some changes and turns into vinegar which is pure. The fuqaha’ also had similar consensus upon this view. Similarly, if a dead body of a pig, falls into the basin of salts, and overtime degraded becomes salt. Thus the final product, which is the salt is consider as pure and clean. The same goes to the animal faeces, unclean body disposal taken and burnt into ashes, thus the burnt ashes is considered as pure too.

### Malikiyy Madhhab

Among the fuqaha scholars of Malikiyy, they also do have similar views upon istihalah issue. Anything which if *najis* and unclean, undergone some changes and the final product is pure and good is considered as pure. While if a pure substance undergone some process and turns into *najis* and unclean, is *najis*. Al imam al-Dusuqiyy (N.d) in his book, “Hashiyat al-Dusuqiyy Ala al-Sharh al-Kabir” wrote:

(وَمُسْكٌ) بِكَسْرِ فَسُكُونٍ وَأَصْلُهُ دَمٌ انْعَقَدَ لِاسْتِحَالَتِهِ إِلَى صَلَاحٍ

Which means, “(A musk) its origin is blood and has undergone istihalah for good purpose (perfumery) is permiseble”.

And Imam ‘Ulaysh (1989) wrote’s in his kitab:

وَعِلَّةُ بَحَاسَةِ الْقَيْءِ الْمُتَغَيَّرِ الْإِسْتِحَالَةُ إِلَى فَسَادٍ

Which means, “The ‘illah (reason) of the impurity of vomiting is its change to something dirty and useless”.

All of them including imam al-Dusuqiyy (N.d) in his book; “Hashiyat al-Dusuqiyy Ala al-Sharh al-Kabir”, did mentioned:

(و) الطَّاهِرُ (صَفْرَاءُ) وَهِيَ مَاءٌ أَصْفَرٌ مُلْتَجِمٌ يُشْبِهُ الصَّبْغَ الرَّعْفَرِيَّ يَخْرُجُ مِنَ الْمَعِدَةِ (وَبَلْغَمٌ) وَهُوَ الْمُنْعَقِدُ كَالْمُخَاطِ يَخْرُجُ مِنَ الصَّدْرِ أَوْ يَسْقُطُ مِنَ الرَّأْسِ مِنْ آدَمِيٍّ أَوْ غَيْرِهِ لِأَنَّ الْمَعِدَةَ عِنْدَنَا طَاهِرَةٌ لِإِعْلَةِ الْحَيَاةِ فَمَا يَخْرُجُ مِنْهَا طَاهِرٌ وَعِلَّةُ بَجَاسَةِ الْفَيْءِ الْإِسْتِحَالَةُ إِلَى فَسَادٍ

Which means, “(Safra’) a concentrated yellow water like za’faran concentrated that comes out from stomach and (balgham) or mucus, a slimy substance, usually not miscible with water, secreted by a mucous membrane or gland that comes out from chest or head of human. These two substances are considered clean as it come out from belly otherwise, the (illah) reason of vomit is unclean (najs) as it is bad facade”.

### HanbaliyyMadhhab

One of the well known scholars, IbnQudamah (N.d) has written in his kitab“al-Mughniyy” as:

ظَاهِرُ الْمَذْهَبِ، أَنَّهُ لَا يَطْهَرُ شَيْءٌ مِنَ النَّجَاسَاتِ بِالِاسْتِحَالَةِ، إِلَّا الْحَمْرُ، إِذَا انْقَلَبَتْ بِنَفْسِهَا خَلًّا، وَمَا عَدَاهُ لَا يَطْهَرُ؛ كَالنَّجَاسَاتِ إِذَا احْتَرَقَتْ وَصَارَتْ رَمَادًا، وَالْحَنْزِيرِ إِذَا وَقَعَ فِي الْمَلَاخَةِ وَصَارَ مِلْحًا، وَالذُّخَانَ الْمُتَرَقِّيَ مِنْ وَقُودِ النَّجَاسَةِ، وَالْبَخَارِ الْمُتَصَاعِدِ مِنَ الْمَاءِ النَّجَسِ إِذَا اجْتَمَعَتْ مِنْهُ نَدَاوَةٌ عَلَى جِسْمٍ صَقِيلٍ ثُمَّ قَطَّرَ، فَهُوَ بَجَسٌ. وَيَخْرُجُ أَنْ تَطْهَرَ النَّجَاسَاتُ كُلُّهَا بِالِاسْتِحَالَةِ قِيَاسًا عَلَى الْحَمْرَةِ إِذَا انْقَلَبَتْ، وَجُلُودِ الْمَيْتَةِ إِذَا دُبِعَتْ، وَالْجَلَالَةَ إِذَا حُبِسَتْ، وَالْأَوَّلُ ظَاهِرُ الْمَذْهَبِ. وَقَدْ نَهَى إِمَامُنَا - رَحِمَهُ اللَّهُ - عَنِ الْحَبْزِ فِي تَنْوِيرِ شُؤْيِ فِيهِ حَنْزِيرٍ

Which means, “It is clear that something that najas will not purified by istihalah, except liquor, if it turns itself into vinegar, otherwise it is not purified; likefilth if burned and transform into ashes, pigs if it was dead on the salt field and then dissolving with the salt, and the smoke from the filth burner, water vapor that rising from the stool if it was accumulated over a cloth and then extracted, then it is najas. And all things that najas will be purified by the qiyas of istihalah in liquor transformed into vinegar, tanned animal skins and jallalah animals (animals that eat carcasses) that being locked in a cage. Our imam (scholar) also forbid us to baked bread in oven that used for roasting pork”.

While Abu al-Khattab al-Kaluzaniyy (2004) in his kitab:“al-Hidayah AlaMadhhab al-Imam Abi Abdillah Ahmad bin Muhammad bin Hanbal al-Shaybaniyy” did mentioned:

وَلَا يَطْهَرُ شَيْءٌ مِنَ النَّجَاسَاتِ بِالِاسْتِحَالَةِ، إِلَّا الْحَمْرُ إِذَا انْقَلَبَتْ بِنَفْسِهَا، فَإِنْ خُلِّتْ لَمْ تَطْهَرُ. وَقِيلَ: تَطْهَرُ وَلَا يَطْهَرُ جِلْدُ مَا لَا يُؤْكَلُ لَحْمُهُ بِالذَّكَاةِ، وَلَا تَطْهَرُ جُلُودُ الْمَيْتَةِ بِالذَّبَاغِ فِي أَصَحِّ الرَّوَايَتَيْنِ، وَالْأُخْرَى يَطْهَرُ مِنْهَا جِلْدُ مَا كَانَ طَاهِرًا فِي حَالِ الْحَيَاةِ

Which means, “And it is not purified from uncleanness with istihalah, except alcohol if it changes naturally, otherwise it is not purified; and some said it is purified. The skin of animal is unclean if it's not slaughtered in Islamic ways. The skin of dead animal is unclean even even its undergone samak process according to strong opinion. And the second opinion said, it cleanses the skin of what was pure (tahir) in the case of it's life”.



## THE CLINICAL APPLICATION OF *ISTIHALAH* CONCEPT IN USING THE LOW MOLECULAR WEIGHT HEPARIN (LMWH)

The concept of *istihalah* as discussed according to the scholars as mentioned above has its own organized definition, to simplify it means any form of a substance that originally considered as the unclean or *najis* by the Islamic law, undergone certain process or changes and become pure as the final product is considered pure and clean. Base on this theory, this concept is very applicable in determining the discussion of clinical application of LMWH as the final end product which is clean and purified. This very important as LMWH is widely used including among the muslim community in treating their medical associated illness in pregnancy.

This medication is used widely due to its proven efficacy and safety profile in the pregnancy as prophylaxis and treatment to ensure healthy mother and baby. Yet the usage has raised concern among muslim communities. Knowing that it originates from porcine guts layers and synthesized into the medication. The process involved was depolymerization procedures where the polymers of proteins from this layers, broken into monomers which is the smallest particles and processed. This process can only be achieved under a very high temperature relatively comparable to any substance that is burnt by the heat.

In Malaysia, the usage of any porcine components within the food, medicine or even cosmetics used widely by the Muslims are seriously taken into and look upon by various Muslim religious bodies. Monitoring of '*halal*' quality including purity of the substance, analysis and even debates among the scholars. The National Fatwa Council had their *muzakarah* upon this sensitive issue of using the porcine based material which had undergone biotechnology process for certain usage by Muslims.

According to their 87<sup>th</sup> '*Muzakarah Jawatankuasa Fatwa Majlis Kebangsaan Bagi Hal Ehwal Ugama Islam Malaysia (MJFMK)*' held on 23<sup>rd</sup> to 25<sup>th</sup> Jun 2009. A discussion was made specifically to discuss regarding the usage of LMWH (porcine based) which included '*Clexane*' '*Fraxiparine*' as compared to '*Arixtra*' synthetic base. The fatwa statement specifically mentioned that it is '*haram*' to use LMWH as there is the availability of other option, which is synthetic base anticoagulant for medicinal purpose.

## DISCUSSION

After almost 10 years since the fatwa was released, there were more recent studies and updates around the world to further explore regarding the usage of LMWH in pregnancy and any possibilities of newer improved drugs. Unfortunately, there were increments of maternal death related to obstetric embolism to date. Principal cause of maternal death is still obstetric embolism in 2016 which was 23% in Malaysia (statistic on Causes of Death Malaysia, 2017). More guidelines and protocols supported with studies on drug safety and efficacy in preventing and treating obstetric embolism has been produced. The evidence has shown that LMWH, has been superior than its synthetic drug companion, *Arixtrain* pregnant patients.

Physiological changes in pregnancy has made these women becomes hypercoagulable than a normal non pregnant woman. With more women embarking into pregnancy at advance age beyond 35 years old and obese population, our risk factors for embolism in pregnancy has increased in general. Further increase in assisted reproductive techniques, surgical procedures and awareness of medical disease which are inherited conditions of abnormalities in the blood which make these women knocking to the door

of death if they gets pregnant. Metabolism changes in a pregnant woman also differ making it very complex in deciding certain treatment, and safety risk to the unborn baby should be considered upon starting a medication. Unfortunately, ethically it is difficult for trials of new drug in pregnant woman.

LMWH has proven to show better safety profile due to its bigger molecular size than Arixtra (fondaparinux) it did not pass through the placenta to fetus. Studies has shown *Fondaparinux* presence in the fetal blood, although according to U.S. Food and Drug Administration (FDA) as category B, we still do not know the impact to the fetus as no proper studies were done. Furthermore, being a synthetic anticoagulant *Fondaparinux* is not metabolised in the body, it requires 100% excretion from the kidney as compare to LMWH which is lower percentage of excretion. Unfortunately kidney excretion in pregnancy has some degree of changes to accommodate the baby. It function easily deteriorate especially women with medical problem in pregnancy such as high blood pressure. Failure of excretion leading to accumulation of this drug in the body resulting danger to both mother and baby as patient may complicate with bleeding problem to death. This condition is not reversible with any medication as it is synthetically produce. Unlike LMWH, it has better safety profile as there is an antidote in cases of bleeding using protamin sulphate. *Fondaparinux* also had longer half life, exposing to higher risk accumulation in the blood. This is the main reason LMWH is the best choice to use in pregnancy as prophylaxis and treatment.

Another factor that is perhaps considerable is that LMWH is far cheaper than *Fondaparinux*. Among all the expertise around the world and even in Malaysia, Obstetricians had gathered consensus that LMWH is far superior better used in pregnancy. More recent updates from the medical lab that is certified by renown religious body in Malaysia is that these LMWH were tested and there were absent porcine elements traced. LMWH has been used widely around the globe by almost all the Muslim obstetric consultants in Islam countries base on *istihalah* concept, similarly in our local setting despite the national fatwa given.

**Figure 2: Comparison Table Between Anticoagulant And Its Properties**

Properties	Enoxaparin Sodium (low molecular weight heparin, LMWH)	Fondaparinux
Source	Porcine intestinal mucosa layer	Synthetic polysaccharides
Molecular weight <i>Dalton (Da)</i>	4500	1728
Half life	5-7 hours	17-21 hours
Renal excretion	High (70%)	High (100%)
Excreted Placenta/ breast milk (RCOG guidelines)	No/ not known but safe in breast feeding as it is not in active form	Not known
Metabolised	Depolymerisation	Not metabolized
Antidote	Reversed with protamine sulphate	Not available
Category in usage to pregnant mother	Category B	Category B

(US FDA)		
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\*Category B: Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

However, the statement above did not mean that these doctors were against the fatwa council. The Islamic medical community are aware regarding this matter and trying to find further prove to help in treating patients and honouring the *deen*. Decision made was always following *maqasid of syariah*, thus according to Dr. Suhazeli Abdullah (2016) as family medicine specialist regarding the usage of LMWH and the fatwa; as much that he agreed with it. The availability and feasibility of the medicine should also be considered especially in *darurah or medical emergency, or there were no alternative as good as it is available*. A discussion regarding this issue was made between him and associate Professor Dr. Basri Ibrahim in venous thromboembolism seminar (Tabung Haji Hotel on the 3<sup>rd</sup> August, 2016) it is permissible usage for pregnant women base on all the safety profile, efficacy and feasibility to date.

Thus, base on all the evidence discussed as above, this review would like to recommend the *hukumas* the following:

1. Base on the clinical studies and data available; the usage of LMWH in pregnant women is permissible.
2. The recommendation should be bound to the rules it is really indicated as been assessed by the consultant obstetrician and there were no other similar drug with similar safety profile and efficacy.

The recommendation were made base on the evidence as follows:

1. Scientific evidence has proven that LMWH *Enoxaparin Sodium (Clexane)* which was mentioned in the fatwa was far superior than *Fondaparinux (Arixtra)*.
2. LMWH has very minimal side effects and possible complications as compare to than *Fondaparinux (Arixtra)*.
3. According to Fiqh method *fiqh "al-Hajah Tunazzal Manzilat al-Darurah: Ammatan Kanat aw Khassah"* which means *Al-Hajah (the necessity)* equivalent to the *darurah* status either it is general use or specific in certain condition; *al-hajah with justification (al-taysir)* and feasibility (*al-tashil*) to use whatever is required. This category is slightly lower than the *darurah* of fatality (Al-Zuhayliyy, Muhammad, 2006 & AlBurnu, 1996). As *darurah* is considered as the reference point between halal and haram, thus the justification includes *al-hajah*. This is base on Shafi'iyya atau Hanbaliyy scholars in istihalah issue *al-hajah* is permissible although it was not a true *darurah*, especially in the usage of LMWH in pregnancy.
4. According to the expert opinion, in this case the obstetricians and medical consultants consensus. According to Dr. Adnan Azayzah (2006), the expert opinion and decision of the usage must be from the person with the verified qualifications, experience and vast knowledge in the related field whereby he is the point of reference of others. Imam al-Nawawiyy (1991), al-Zayla'iyy (1982), al-Kasaniyy (1986), al-Mawwaq (1994) dan Ibn Muflih (1997) mentioned the same thing in their books. Therefore; the opinion of the obstetricians should be considered in this issue.

5. The raised issue regarding porcine based LMWH and *istihalah* is a fiqh arguments or *khilafin thefiqh* concept. It was not an issue base on Hanafiyy or Malikiyy scholars as *istihalah* is well accepted. Yet, according to Shafi'iy scholars which is the majority in our country, atau Hanbaliyy; we would like to propose permissible with terms and conditions as mentioned in the discussion base on *al-hajah*.

Similar *istihalah* concept has been used and applied in other Muslim countries by their religious body. As example, the Singaporean Islamic body (Majlis Ugama Islam Singapura) in the usage of porcine based trypsin enzyme used for vaccination preparation. The enzyme was the safest method to produce the vaccine, which then after undergone many procedures until the final vaccine product only had 0.001% trace of porcine element. Thus, it is permissible base on *istihalah* fiqh concept to use this vaccine (Naziruddin Mohd Nasir, N.d). Similar concept by Dar al-Ifta' al-Misriyyah in producing fatwa upon the permissibility of using any food with presence of non halal elements (porcine or non slaughtered animals) which undergone many process and become purified. ([dar-alifta.org](http://dar-alifta.org), n.d).

## CONCLUSION

The *istihalah* concept is very much relevant *fiqh* method to be used these days especially in many products or substance with non halal or unclean elements which had undergone many stages of process until purified. This is concurrent with the technology advancement in treating and improving health among mankind. Yet the application should be carefully looked upon by Muslim scholars so that it will not be too liberal or too conservative in making decision (Zaharuddin Abdul Rahman, 2015).

After thorough discussion, reviewing the new emerging evidences which clearly shows the benefit and higher safety profile of LMWH to be use among selected pregnant women with risk of venous thromboembolism as prevention and debates between scholars, the usage of porcine based LMWH can be permissible among selected pregnant women with risk as preventive medicine using the *istihalah* method.

However, as it is against the previous national fatwa statement, a consensus between the muslim scholars and medical expert are very much obliged to revise it and to decide the *istihalah* concept and its *hukum* upon this matter as more evidence and data have emerged. Perhaps more solutions can be offered on every new issue similar as our discussion.

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