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ORIGINAL ARTICLE

Prevalence and associated factors of lipohypertrophy in insulin-injected patients with diabetes in selected primary care clinics in Peninsular Malaysian: A cross-sectional study

Siti Hawa Alias, Cheong Lieng Teng, Navin Kumar Devaraj, Saadatunnoor Amirrudin, Noor Rawaida Abd Latib, Fui Yee Chong, Syamimi Yussof, Mohamad Danial Mohamad Din, Poon Wah Lim

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Authors:

Siti Hawa Alias
(Corresponding author)
MBBS (IIUM), FRACGP (Australia)
Klinik Kesihatan Port Dickson, Port Dickson, Negeri Sembilan Malaysia.
Email: sitihawaalias85@gmail.com

Cheong Lieng Teng
MBBS (UM), MFamMed (FRACGP)
Department of Family Medicine, International Medical University (IMU), Jalan Rasah, Bukit Rasah Seremban, Negeri Sembilan, Malaysia.

Navin Kumar Devaraj
MD (UPM), MFamMed (Malaya)
Department of Family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, Malaysia.

Saadatunnoor Amirrudin
MBBS (IIUM), FRACGP (Australia)
Klinik Kesihatan Seremban 2, Seremban, Negeri Sembilan, Malaysia.

Abstract

Introduction: This study aimed to determine the prevalence and associated factors of lipohypertrophy in insulin-injecting patients with diabetes at selected primary care clinics in Malaysia.

Methods: This cross-sectional study was conducted among adults aged ≥18 years with type 1 or 2 diabetes treated with insulin for at least 6 months at six selected public primary care clinics in Malaysia. The Injection Technique Questionnaire was used, and physical examination was conducted to detect the presence of lipohypertrophy. Univariate and multivariate logistic regression analyses were conducted using IBM SPSS version 26.

Results: A total of 506 patients with type 2 diabetes were included in this study; of them, 60.47% were women, and 48.42% were Malays. The prevalence of lipohypertrophy was 39.6% (95% Confidence Interval, CI =35%–44%). The univariate analysis revealed that a larger number of injections per day, longer needle length, repeated use of needles, incorrect rotation of the injection site, longer insulin use duration, higher total insulin dose and higher HbA1c level were significantly associated with lipohypertrophy. In the multivariate logistic regression analysis, incorrect rotation of the injection site was the only independent associated factor of lipohypertrophy.

Conclusion: The prevalence of lipohypertrophy in this study is comparable with that in other studies. The identified associated factors of lipohypertrophy must be addressed in ongoing health education for insulin-injecting patients at Malaysian primary care clinics. Educating healthcare professionals and increasing awareness among patients with diabetes are important steps in preventing this complication.

Introduction

The National Health and Morbidity Survey 2019 indicated that the prevalence of diabetes among adults in Malaysia increased from 13.4% in 2015 to 18.3% in 2019.[1] In Malaysia, approximately 400,000 out of 1.6 million (25.1%) patients with known diabetes were using insulin.[2] According to the Malaysian National Diabetes Registry, insulin use in primary care settings had almost doubled from 2009 to 2012 (rising from 11.7% to 21.4%).[3] Insulin-injecting patients may develop treatment-related complications such as allergy, lipohypertrophy, hypoglycaemia and, rarely, oedema.[4]

Lipohypertrophy is a thickened, rubbery lesion that is formed when injections of insulin are given repeatedly at the same location.[4,5] Repeated insulin injection causes microtrauma and, together with the growth-promoting effect of insulin on the repairing cell, can result in hypertrophy of adipose tissue at the trauma site. Subsequently, lipohypertrophy forms over the trauma site over time. This lesion is aggravated with needle reuse.[4,5] Lipohypertrophic areas may be visible and/or palpable, and some lesions may be easily felt rather than visualised.[6]

Lipohypertrophy has many undesirable effects, ranging from skin disfigurement to impairment of insulin absorption. Insulin absorption is usually reduced or delayed, resulting in an increased requirement of the total daily dose

Noor Rawaida Abd Latib
MBChB (Otago), FRACGP (Australia)
Klinik Kesihatan Sendayan, Jalan Felda Sendayan, Seremban, Negeri Sembilan, Malaysia.

Fui Yee Chong
MD (UNIMAS), FRACGP (Australia)
Klinik Kesihatan Sepang, Jalan Kelap, Sepang, Selangor, Malaysia.

Syamimi Yussof
MBBS (Bangalore), FRACGP (Australia)
Klinik Kesihatan Merlimau, Jalan Muhibbah 9a, Merlimau, Melaka, Malaysia.

Mohamad Danial Mohamad Din
MBBS (Bangalore)
Poliklinik & Surgeri Merlimau, Merlimau, Melaka, Malaysia.

Poon Wah Lim
MD (Ukraine),
Klinik Sidhu, Kampung Tok Ungku, Seremban, Negeri Sembilan, Malaysia.

of insulin and its associated costs. One study conducted in China has estimated that the additional insulin needed in patients with lipohypertrophy compared with those without lipohypertrophy is 15 IU per day.[7]

Deng et al.[8] systematically reviewed 26 palpation-based cross-sectional studies and found wide differences in the prevalence of lipohypertrophy (1.9%–73.4%). Among these studies, three included patients with type 2 diabetes,[9–11] and only one was conducted at a primary care clinic (a hospital-based study in Saudi Arabia).[8]

In the Worldwide Injection Technique Questionnaire (ITQ) Study conducted in 42 countries involving 13,289 insulin-injecting patients, the overall prevalence of lipohypertrophy was 30.8%.[12] The ITQ study identified several risk factors of lipohypertrophy, including longer duration of insulin use, poorer glycaemic control, glycaemic variability and unexplained hypoglycaemia.[12,13]

In view of the absence of relevant data in the Malaysian primary care setting for insulin-injecting patients with diabetes, the present study was conducted to determine the prevalence and associated factors of lipohypertrophy in this setting.

Methods

Study design, setting and participants

This cross-sectional study was conducted among adult patients with type 1 or 2 diabetes who had been treated with insulin for at least 6 months. In the literature search for major studies in this field including the Worldwide ITQ Study, no study has been found to evaluate the duration of the development of lipohypertrophy after starting insulin injection therapy. In the present study, pregnant patients with diabetes were excluded. The study was conducted at six public primary care clinics in central Peninsular Malaysia. Four of the study sites were located in urban areas and the other two in suburban areas. These study sites were selected because of convenience and logistic reasons.

In the study sites, diabetes care (including insulin therapy) is delivered by a medical officer under the supervision of family medicine specialists. Insulin-filled pen is prescribed in accordance with the national clinical practice guidelines on diabetes and insulin therapy.[14,15] The cost of medical treatment is heavily subsidised (RM 1 for consultation, laboratory tests and drugs; however, consumables such as insulin needles and glucometer test strips are not provided).

The study respondents were recruited via systematic sampling wherein we sampled every one out of three patients who attended the clinic that day from September to November 2019 until the sample size was achieved.

The sample size was based on the prevalence of lipohypertrophy in the ITQ study (30.8%), yielding a sample size for this study of 323 respondents. A 50% larger sample size was needed to include the associated risk factors of lipohypertrophy; this yielded a required sample size of 485 respondents.

Study questionnaire and data collection

The study questionnaire was adapted from the Worldwide ITQ Study.[12] The questionnaire was made available via the Fitter4Diabetes website. There are 17 language versions of the questionnaire including the Malay version, which had been validated and used in two tertiary centres in Malaysia as part of the Worldwide ITQ Survey in 2014. Permission to use the questionnaire was obtained.

The questionnaire was divided into two sections: Section A focused on the demographic data of respondents, and Section B comprised questions assessing the factors associated with the development of lipohypertrophy in insulin-injecting patients with diabetes (**Appendix A**). The questionnaire was written in both English and Malay, but its application was interviewer-assisted in some respondents.

Physical examination was performed on the insulin injection sites by the study investigators to detect the presence of lipohypertrophy. All researchers had attended the training course 'Forum for Injection Technique Malaysia', which emphasised the detection of lipohypertrophy via both inspection and palpation prior to data collection.

Ethical approval and funding

This study received ethical approval from the Medical Research and Ethics Committee of the Malaysian Ministry of Health and was funded by the Academy of Family Physicians of Malaysia. It was conducted in accordance with the Code of Ethics of the World Medical

Association (Declaration of Helsinki). All study respondents provided written informed consent prior to enrolment in the study.

Statistical analysis

Data were analysed using IBM SPSS version 26.0. The main outcome variable was the occurrence of lipohypertrophy. Correct injection site rotation was defined as injection at at least 1 cm from other previous injection sites.5 Continuous variables were reported as means and standard deviations (SDs) and categorical variables as frequencies and percentages. A univariate analysis was performed using the chi-square test or t-test. Factors with a P-value of <0.05 in the univariate analysis were entered into a logistic regression model to determine the factors independently associated with lipohypertrophy. The statistical significance level was set at P<0.05.

Results

Demographic and clinical characteristics of the participants

A total of 506 adults with type 2 diabetes were enrolled in this study. **Table 1** shows their demographic and clinical characteristics. None of the respondents had type 1 diabetes. Most respondents were aged ≥60 years (51.4%). Almost two thirds had diabetes for ≥10 years (63.2%), and almost half had been on insulin therapy for ≥5 years (45.1%). The mean insulin dose was 0.67 units per kg (SD=0.41). Most respondents did not have optimal glycaemic control; only 15.2% achieved an HbA1c level of ≤7% (53 mmol/mol).

Table 1. Demographic and clinical characteristics of the study respondents.

Characteristics	Number of respondents (%)	Mean (SD *)
Sex		
Male	200 (39.53)	
Female	306 (60.47)	
Ethnicity		
Malay	245 (48.42)	
Chinese	93 (18.38)	
Indian	167 (33.00)	
Others	1 (0.20)	
Age, year		59.31 (10.81)
Duration of diabetes, year		12.58 (6.96)
Body mass index, kg/m2		28.21 (5.88)
Latest HbA1c level, %		9.29 (2.11)
Type of medication		
Oral antidiabetic agent	435 (85.97)	
Biguanides	431 (85.18)	
Sulphonylureas	95 (18.77)	
Dipeptidyl peptidase-4 inhibitors	6 (1.19)	
Injectable insulin	506 (100)	
Short-acting insulin	182 (36.00)	
Rapid-acting insulin	5 (1.00)	
NPH insulin	268 (52.96)	
Long-acting insulin	19 (3.75)	
Pre-mixed insulin	212 (41.90)	
Frequency of home blood glucose monitoring		
3–4 times a day	16 (3.16)	
1–2 times a day	55 (10.87)	
Several times a week	176 (34.78)	
Rarely or never	259 (51.19)	
Duration of insulin use, year		4.76 (3.82)
Total insulin dose, unit		48.11 (29.26)

*SD= standard deviation

No patients were prescribed meglitinides, alpha-glucosidase inhibitors, thiazolidinediones or sodium–glucose cotransporter 2 inhibitors.

Occurrence and associated factors of lipohypertrophy

Physical examination revealed that 200 participants had lipohypertrophy, yielding a prevalence of 39.5% (95% CI=35.2%–43.9%). The sizes of lipohypertrophy varied from 5 to 60 mm (mean=17.07±11.88). Approximately one fifth of the participants (38/200, 19.0%) realised that they had lipohypertrophy. Among those who were found to have lipohypertrophy (n=200), 158 (79%) admitted that they had injected their insulin into the lump.

As shown in **Table 2**, lipohypertrophy was significantly more common with a larger number of injections, longer needle length and increased frequency of repeated use of needles. Among the participants who reported rotating their insulin injection site (n=429), lipohypertrophy was significantly more common in those who were found to have an incorrect rotation of the injection site.

Table 2. Association of the categorical variables with the occurrence of lipohypertrophy.

Variables	Lipohypertrophy, n (%)	Total number of respondents	Statistics
Number of injections per day			
1	32 (29.63)	108	χ^2=25.43, P<0.001*
2	82 (33.88)	242	
3	2 (18.18)	11	
4	84 (57.93)	145	
Length of needle (mm)			
4	91 (34.73)	262	χ^2=12.97, P<0.001*
5	51 (36.17)	141	
6	52 (54.74)	95	
8	6 (75.00)	8	
Repeated use of needle (time)			
None	6 (10.00)	60	χ^2=35.71, P<0.001*
2	45 (34.35)	131	
3–5	110 (43.48)	253	
6–10	28 (63.64)	44	
>10	11 (61.11)	18	
Rotation of injection site**			
Yes	170 (39.63)	429	χ^2=0.054, P<0.816*
No	30 (42.86)	77	
Correct rotation of injection site***			
Yes	10 (6.37)	157	χ^2=114.48, P<0.001
No	160 (58.82)	272	

*Chi-square test for trend
**Based on the respondents' report
***Based on correct site rotation practice – injection at at least 1 cm from the previous injection site (n=429)

As shown in **Table 3**, lipohypertrophy was significantly more common among the participants with a longer insulin use duration, higher total insulin dose and higher HbA1c level than among the other participants.

Table 3. Association of the categorical variables with the occurrence of lipohypertrophy.

Variables	Lipohypertrophy present	Lipohypertrophy absent	Statistics
Insulin use duration, year	5.49 (SD=3.96)	4.29 (SD=3.65)	t=3.51, df=504, P<0.001
Total insulin dose, unit	55.30 (SD=30.92)	43.42 (SD=27.16)	t=4.55, df=504, P<0.001
Most recent HbA1c level, %	9.77 (SD=2.15)	8.98 (SD=2.04)	t=4.14, df=504, P<0.001
Most recent HbA1c level, mmol/mol	83 (SD=23)	75 (SD=22)	t=4.14, df=504, P<0.001

Table 4 illustrates the factors associated with the presence of lipohypertrophy; the variables found to be significant in the univariate analysis (Tables 2 and 3) were added to the logistic regression model. In the multivariate analysis, we found that incorrect rotation of the injection site was the only factor that had a significant association with the occurrence of lipohypertrophy. The seven variables in the logistic regression model could explain approximately 32%–44% of the variation in the occurrence of lipohypertrophy (Cox–Snell R2=32.1%; Nagelkerke R2=43.5%).

Table 4. Multivariate analysis of the factors associated with lipohypertrophy.

	B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)	
							Lower	Upper
Insulin duration, year	0.079	0.037	4.530	1	0.033	1.083	1.006	1.165
Number of injections per day	0.211	0.147	2.056	1	0.152	1.235	0.926	1.647
Needle length (reference=4 mm)			5.906	3	0.116			
8 mm	1.498	0.963	2.417	1	0.120	4.472	0.677	29.550
6 mm	0.578	0.316	3.338	1	0.068	1.782	0.959	3.313
5 mm	0.436	0.302	2.086	1	0.149	1.546	0.856	2.794
Frequency of needle reuse (reference=none)			4.200	4	0.380			
2 times	0.626	0.634	0.973	1	0.324	1.869	0.539	6.477
3–5 times	0.553	0.608	0.828	1	0.363	1.739	0.528	5.721
6–10 times	1.254	0.701	3.203	1	0.074	3.504	0.888	13.832
>10 times	0.896	0.863	1.077	1	0.299	2.449	0.451	13.295
Total insulin dose per day, unit	0.004	0.006	0.421	1	0.517	1.004	0.992	1.015
Incorrect rotation	3.023	0.367	67.797	1	0.000	20.561	10.011	42.226
Most recent HbA1c level	0.035	0.058	0.363	1	0.547	1.036	0.924	1.162
Constant	–4.991	0.901	30.716	1	0.000	0.007		

Cox–Snell R^2=32.1%; Nagelkerke R^2=43.5%
Hosmer and Lemeshow test: χ^2=10.65, df=8, P=0.223

Discussion

In this study, lipohypertrophy was detected in 39.5% of the insulin-injecting patients with type 2 diabetes. This prevalence is close to that reported in the Worldwide ITQ Study (30.8%)[12,13] as well as in the meta-analysis conducted by Deng et al.[8] (38%).

The factors found to be significantly associated with the occurrence of lipohypertrophy in our study included the following: larger number of injections per day, longer needle length, repeated use of needles, incorrect rotation of the injection site, longer insulin use duration, higher total insulin dose and higher HbA1c level (Tables 2 and 3). All of these factors have also been found to be associated with lipohypertrophy in other studies.[9,10,13,16] Taken together, these factors match the current understanding of the aetiopathogenesis of lipohypertrophy (i.e. injection trauma and persistent exposure of the injection site to insulin).

In our multivariate logistic regression analysis, only incorrect rotation of the injection site remained significant, whereas all other factors were not independently associated with the occurrence of lipohypertrophy. In actual clinical practice, lipohypertrophy is caused by multiple factors; hence, a multivariate logistic regression analysis is a good approach because it mimics reality compared with a univariate analysis. A closer examination of the results of other studies revealed that incorrect rotation was also found to be the strongest risk factor for lipohypertrophy, although other several variables were also significant in those studies.[9,10,13,16]

Our study findings point to the importance of assessing the injection technique of insulin-injecting patients with diabetes under our care. In view of the multiple errors in their injection technique, a strong case can be made with regard to education and training in our setting. Previous interventional studies conducted in France and the United Kingdom showed that education and training can correct specific errors such as repeated use of needles and choice of appropriate needles (4 mm being the preferred length in adults) and can emphasise the importance of correct rotation of the injection site.[17,18]

The most important factor promoting lipohypertrophy in our study was the incorrect rotation of the injection site. Thus, there is a need for continuous appropriate education and training for both patients and healthcare professionals.

Malaysian public primary care services mostly cater low- and middle-income populations; hence, consultation fees and treatment charges are heavily subsidised (an adult Malaysian citizen pays RM 1 or USD 0.25; for those aged ≥60 years, this fee is waived). However, consumables such as insulin needles and glucometer test strips need to be purchased by patients on their own. Thus, it is expected to find a relatively low frequency of home blood glucose monitoring (**Table 1**) and high frequency of repeated use of insulin needles (**Table 2**). In view of these findings, some challenges with regard to the recommended best practice of single use of insulin needles are anticipated.

Primary care centres are an uncommon setting to be included in lipohypertrophy studies. We noted that the only primary care-based study conducted to date is that by Al Ajlouni et al.[9], which reported a prevalence of lipohypertrophy of 37.3%. To our knowledge, the present study is the first to be conducted at six primary care clinics in Malaysia involving a large number of respondents representing central Peninsular Malaysia, making this our study's strength.

There are a few limitations in our study. Our study respondents were recruited from only the six selected public primary care clinics (out of 900 such clinics in the entire country). Although the study clinics were not randomly selected, the characteristics of the study respondents are fairly similar to those of typical insulin-injecting patients with diabetes. Further, some components of the questionnaire (e.g. insulin use duration and insulin dosage) were based only on self-reports; thus, the possibility of recall bias cannot be excluded. Since the detection of lipohypertrophy was based on physical examination, the varying experiences of the investigators in this study could have yielded some detection bias despite the training provided.

Conclusion

Our study found that the prevalence of lipohypertrophy in insulin-injecting patients with diabetes was 39.5%, which is close to that reported in the Worldwide ITQ Study. An incorrect rotation of the insulin injection site was the most significant modifiable factor associated with lipohypertrophy. Therefore, education on the correct rotation of the insulin injection site must be emphasised. More larger-scale studies should be conducted in the future.

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Author contributions

All authors contributed in data collections and technical input in this writing.

Ethical approval

Ethical approval from the Medical Research and Ethics Committee of the Ministry of Health Malaysia was obtained (NMRR-18-3690-44920) on 25 June 2019.

Conflicts of interest

The authors declare no conflicts of interest.

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Data sharing statement

Data are available upon request.

How does this paper make a difference in general practice?

- This study provides the first local primary care data regarding the prevalence of lipohypertrophy in Malaysia.
- This paper highlights the high prevalence and main associated factors of lipohypertrophy in insulin-injecting patients followed up at primary care clinics in Malaysia.
- The findings suggest the need to revise the formal teaching of insulin injection techniques to patients to include the detection of lipohypertrophy and avoidance of its risk factors.
- This study also identifies the need to educate healthcare professionals on detecting lipohypertrophy in insulin-injecting patients early to ensure better glycaemic control.

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Appendix 1

Questionnaire for Patients with Diabetes who Injecting Insulin

Soalselidik ini adalah secara sukarela dan sulit. Jika anda tidak mahu turut serta, rawatan anda tidak akan terjejas. Pesakit yang telah menggunakan insulin untuk sekurang-kurangnya 6 bulan dijemput menyertai kajian ini. Maklumat yang diberi akan digunakan untuk penambahbaikan latihan dan pendidikan semua yang menggunakan suntikan sebagai rawatan diabetes.

This questionnaire is voluntary and completely anonymous. If you choose not to participate your treatment will not be affected in any way. Persons who have injected insulin or another diabetes medicine for at least 6 months are invited to participate. The information you provide will be used to improve training and education for all people giving injections to manage their diabetes.

1. *Jantina* / Sex? □ *Perempuan* / Female □ *Lelaki* / Male

2. *Umur* / Age? _____ *Tahun* / Years

3. *Berat* / Weight? _____ *kg*

4. *Tinggi* / Height? _____ *cm*

5. How long have you had diabetes?
- □ *6 bulan sehingga 1 tahun – catatkan berapa bulan :* _____*bulan*
  6 months to 1 year - indicate number of months: _____ months
- □ *Lebih daripada 1 tahun – catatkan bilangan tahun:* _____*tahun*
  more than 1 year - indicate number of years: ____ year(s)

6. *Berapakah umur anda sewaktu anda disahkan menghidapi diabetes?* ____ *tahun*
How old were you when you were diagnosed with diabetes? _____years

7. *Ubat yang manakah anda sedang ambil untuk rawatan diabetes (dan telah berapa lama?)*
Which type of treatment are you currently taking for your diabetes (and how long)?
(tick all answers that apply)
- □ *Pil (_____tahun atau _____bulan)*
  Pills (_____years or _____months)
- □ *Insulin (_____tahun atau _____bulan)*
  Insulin (_____years or _____months)
- □ *GLP-1 receptor agonist seperti Byetta atau Victoza (____tahun atau ____bulan)*
  GLP-1 receptor agonist such as Byetta or Victoza (_____years or ____months)

8. *Berapakah jumlah suntikan yang anda cucuk dalam sehari?* /
How many total injections to you give per day?
- □ 1
- □ 2
- □ 3
- □ 4
- □ 5
- □ 6
- □ 7
- □ *Lebih daripada 7* / More than 7

9. *Berapa panjang jarum suntikan yang anda gunakan sekarang?*
What length of needle do you currently use to inject?
□ 8 mm
□ 6 mm
□ 5 mm
□ 4 mm

10. *Bahagian badan yang manakah yang anda gunakan untuk tapak suntikan (tandakan semua jawapan yang berkaitan)? /*
What injection sites do you use (tick all relevant answers)?
□ *Perut* / Abdomen
□ *Paha* / Thigh
□ *Punggung* / Buttocks
□ *Lengan* / Arm

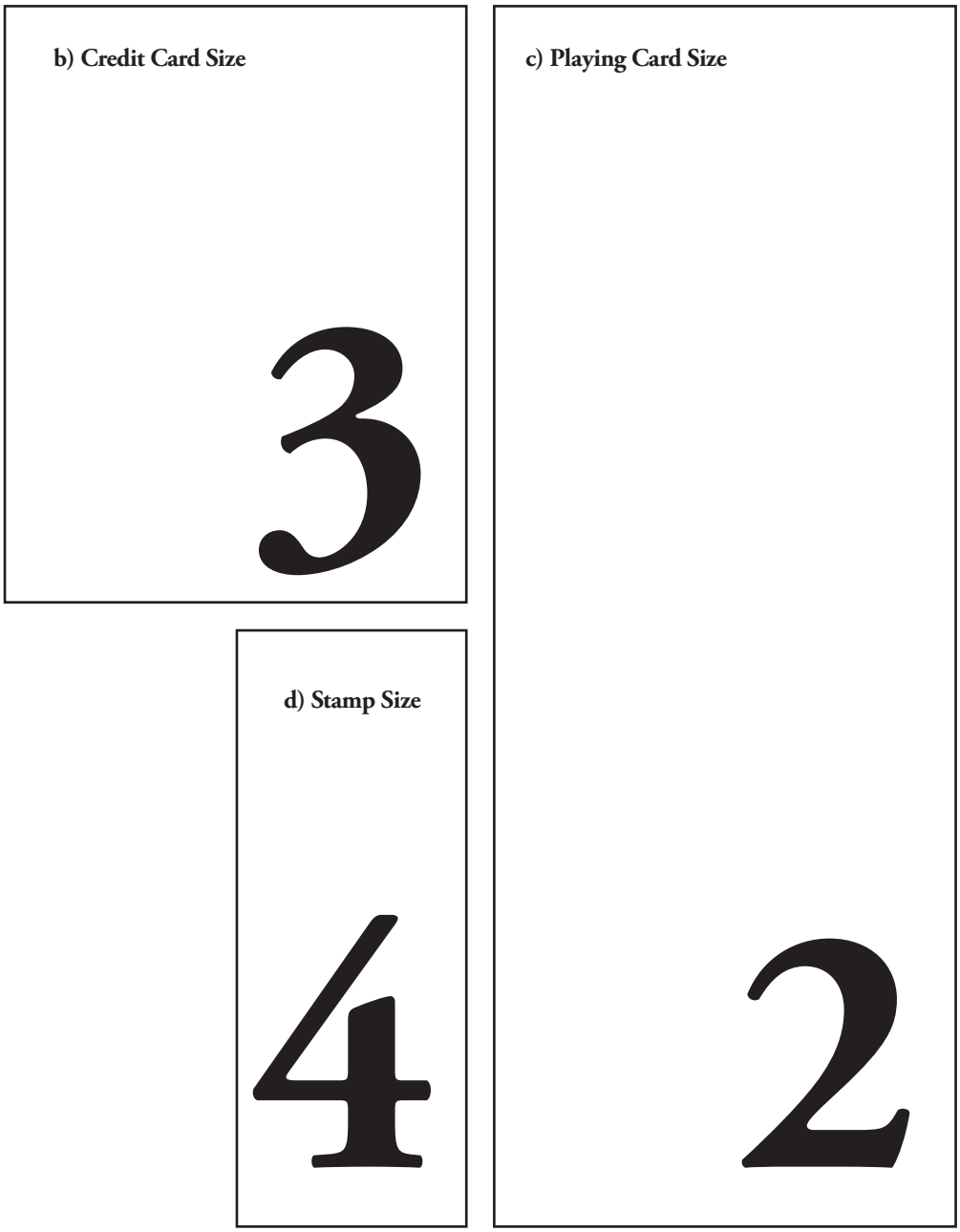
11. *Jika anda menggunakan lebih daripada satu tapak suntikan, rank 1 hingga 4 mengikut kekerapan tempat suntikan tersebut digunakan :* paling kerap = 1, kedua kerap = 2, dan seterusnya /
If you use more than one site rank them 1 to 4 according to frequency used: most often = 1, 2nd most often = 2, etc.?
_____ *Perut* / Abdomen
_____ *Paha* / Thigh
_____ *Punggung* / Buttocks
_____ *Lengan* / Arm

Di dalam soalan 11, anda telah menamakan tapak suntikan yang telah digunakan. Dari kotak-kotak dibawah yang ditunjukkan, pilih kotak yang menggambarkan luas kawasan suntikan anda.

In question 11, you specified the injection sites you use. From the boxes below, choose the one that most closely represents the size of the area of your injections:

	1	2	3	4
Abdomen	□	□	□	□
Thigh	□	□	□	□
Buttocks	□	□	□	□
Arm	□	□	□	□

a) Post Card Size



12. *Bagaimana anda memilih tapak suntikan?* / How do you choose where to inject?

- □ *Saya sentiasa suntik pada tapak yang sama pada masa yang sama setiap hari (contoh : waktu pagi di perut)* / I always inject in the same site at the same time of day (e.g. morning injection always in the abdomen)
- □ *Saya cucuk ditapak yang sama sepanjang hari* / I inject in the same site for a whole day
- □ *Saya cucuk ditempat yang sama untuk beberapa hari* / I inject in the same site for a few days
- □ *Saya pilih tapak suntikan mengikut aktiviti fizikal* / I choose the site according to my physical activity
- □ *Saya pilih tapak suntikan mengikut jadual pusingan* / I choose the site according to my rotation schedule (or plan)
- □ *Saya tiada rutin khas untuk tapak suntikan* / I have no specific injection routine regarding injection site
- □ *Saya pilih bahagian yang paling kurang sakit* / I choose the site that hurts the least
- □ Others: _____

13. *Adakah anda membuat pusingan tapak suntikan?* / Do you rotate injection sites?
- □ *Ya* / Yes
- □ *Tidak* / No

14. *Jika ya, bagaimanakah anda membuat pusingan tersebut?(tandakan semua yang berkenaan)* / If yes, how would you describe this rotation (tick all answers that are correct)?
- □ *Saya ulang-alik dari kiri ke kanan badan* / I move back and forth from right side of my body to left
- □ *Saya pusing dari satu tapak ke satu tapak yang lain* / I move from one injection site to another
- □ *Saya cucuk dangan jarak 1cm dari tempat cucuk sebelumnya* / I inject about a finger's breadth (1 cm) from where I previously injected
- □ *Saya gambarkan suntikan sebagai bulatan pada kawasan suntikan* / My injections describe a circle around my injection sites
- □ *Saya gambarkan suntikan sebagai garisan pada kawasan suntikan* / My injections describe lines across my injection sites.

15. *Adakah terdapat bonjolan atau ketulan dibawah kulit kawasan suntikan biasa anda yang telah lama (minggu, bulan, atau tahun)?*
Do you have any swelling or lumps under the skin at your usual injection sites that have been there for some time (weeks, months or years)?
- □ *Ya* / Yes
- □ *Tidak* / No
- □ *Tidak tahu* / Don't know

16. *Jika ya, ditapak mana?* / If yes, at which site(s)?
- □ *Perut* / Abdomen
- □ *Paha* / Thigh
- □ *Punggung* / Buttocks
- □ *Lengan* / Arm
- □ *Tidak tahu* / Don't know

17. *Adakah anda cucuk di bahagian bonjolan atau ketulan?* / Do you inject into these swellings or lumps?
- □ *Selalu* / Always
- □ *Kadang-kadang* / Sometimes
- □ *Tidak pernah* / Never
- □ *Tidak tahu* / Don't know

18. *Jika ya, tandakan mengapa anda cucuk di bahagian tersebut?(tandakan yang berkenaan)* / If yes, please indicate why you inject into them (tick all that are appropriate)
- □ *Mudah* / It's convenient
- □ *Kurang sakit* / It's less painful
- □ *Sudah biasa* / Just a habit (I always inject there)
- □ *Tidak tahu* / Don't know

19. *Berapa lamakah anda kekalkan jarum dibawah kulit selepas menekan penyuntik?* / How long do you leave the needle under the skin after you have pushed the plunger in?
- □ *< 5 saat* / sec
- □ *5 – 10 saat* / sec
- □ *> 10 saat* / sec
- □ *Saya tidak pasti berapa lama* / I'm not aware of how long

20. *Adakah anda menggunakan jarum lebih dari sekali?* / Do you use your pen needle more than one time?
- □ *Ya* / Yes
- □ *Tidak* / No

21. *Jika ya, berapa kalikah anda menggunakan satu jarum pen?* / If yes, how many times do you use a single pen needle?
- □ *2 kali* / times
- □ *3 - 5 kali* / times
- □ *6 - 10 kali* / times
- □ *> 10 kali* / times

22. *Jika anda menggunakan jarum pen lebih daripada sekali, kenapa anda melakukannya? (tandakan jawapan yang berkenaan)*
If you use the pen needle more than 1 time, why do you do it (tick all appropriate answers)?
- □ *Kerana tiada jarum yang lain* / Because you did not have another pen needle available
- □ *Untuk menjimatkan wang* / To save money
- □ *Untuk menggelakkan pembaziran (bimbang tentang alam sekitar)* / To prevent excess waste (environmental concern)
- □ *Untuk kemudahan sendiri* / For convenience

23. *Adakah suntikan anda menyakitkan?* / Are your injections ever painful?
- □ *Ya* / Yes
- □ *Tidak / No*

24. *Jika ya, terangkan kesakitan tersebut sebaik yang boleh?* / If yes, how would you best describe your injections?
- □ *Sentiasa sakit* / Always painful
- □ *Selalu sakit (beberapa kali seminggu)* / Often painful (several times a week)
- □ *Kadang-kadang sakit (beberapa kali sebulan)* / Sometimes painful (several times a month)
- □ *Hampir tidak pernah sakit (beberapa kali setahun)* / Almost never painful (several times a year)

25. *Apabila suntikan tersebut menyakitkan, apakah pendapat anda punca kesakitan tersebut? (tandakan jawapan yang berkenaan)* / When you have a painful injection, what do you attribute it to? (tick all that may be appropriate)
- □ *Tapak suntikan (contoh : terkena urat saraf)* / The injection site (e.g. I hit a nerve)
- □ *Jumlah insulin yang disuntik* / The amount or volume injected
- □ *Saya telah menggunakan jarum yang sama sebelum ini* / I've already used the needle before
- □ *Cara suntikan saya tidak betul* / My injection technique wasn't right
- □ *Suhu ubat yang disuntik* / The temperature of drug injected
- □ *Saya tidak tahu* / I don't know

26. *Adakah tapak suntikan anda pernah berdarah atau lebam?* / Do your injection sites ever bleed or look bruised?
- □ *Ya* / Yes
- □ *Tidak / No*

27. *Jika ya, berapa kerapkah suntikan tersebut menyebabkan luka atau lebam* / If yes, how often does the injection cause bleeding or bruising?
- □ *Sentiasa* / Always
- □ *Selalu (beberapa kali seminggu)* / Often (several times a week)
- □ *Kadang-kadang (beberapa kali sebulan)* / Sometimes (several times a month)
- □ *Hampir tidak pernah (beberapa kali setahun)* / Almost never (several times a year)

28. *Pernahkah insulin meleleh keluar dari kulit selepas suntikan?* / Does insulin ever leak **out of your injection** site on the skin?
- □ *Ya* / Yes
- □ *Tidak* / No

29. *Jika ya, berapa kerap cecair meleleh dari kulit selepas suntikan?* / If yes, how often does fluid leak out of the skin from the injection site?
- □ *Sentiasa* / Always
- □ *Selalu (beberapa kali seminggu)* / Often (several times a week)
- □ *Kadang-kadang (beberapa kali sebulan)* / Sometimes (several times a month)
- □ *Hampir tidak pernah (beberapa kali setahun)* / Almost never (several times a year)

30. *Pernahkah anda terlepas atau meninggalkan suntikan?* / Do you ever miss or skip an injection?
- □ *Ya* / Yes
- □ *Tidak* / Noe

31. *Jika ya, berapa kerap ia berlaku?* / If yes, how often does this happen?
- □ *Kerap (beberapa kali seminggu)* / Often (several times a week)
- □ *Kadang-kadang (beberapa kali sebulan)* / Sometimes (several times a month)
- □ *Hampir tidak pernah (beberapa kali setahun)* / Almost never (several times a year)

32. *Apakah sebab biasa untuk meninggalkan suntikan? (tandakan semua yang berkenaan)* / What is/are the usual reason(s) for skipping an injection? (tick all that apply)
- □ *Saya lupa* / I forgot
- □ *Saya tidak makan* / I didn't eat
- □ *Saya sakit (contoh : mual dan muntah)* / I was sick (e.g. nausea and vomiting)
- □ *Saya tidak mahu suntik* / I just didn't want to inject
- □ *Paras gula dalam darah saya rendah* / My glucose was too low

33. *Siapakah yang telah mengajar and acara melakukan suntikan? (tandakan yang berkenaan)* / Who taught you how to give your injections? (Tick that all apply)
- □ *Jururawat* / Nurse
- □ *Doctor am* / Doctor
- □ *Doctor Pakar Diabetes* / Doctor (Diabetes Specialist)
- □ *Pegawai farmasi* / Pharmacist
- □ *Wakil dari pengilang pen atau jarum* / A representative of the pen or needle manufacturer

34. *Berapa kerap jururawat atau doctor memeriksa tapak suntikan anda?* / How often does the nurse or doctor examine your injection sites?
- □ *Secara rutin pada setiap kali temujanji. Nyatakan berapa kerap : _____ bulan* / Routinely every visit. Specify how often this is: every_____months
- □ *Setahun sekali* / Once a year
- □ *Hanya jika saya mengadu ada masalah pada tapak tersebut* / Only if I complain of a problem at a site
- □ *Saya tidak ingat yang tapak suntikan pernah diperiksa* / I can't remember my sites ever being checked

35. *Bilakah kali terakhir anda menerima atau menyemak semula arahan suntikan?* / When was the last time you received or reviewed instructions on injections?
- □ *Dalam 6 bulan terakhir* / Within the past 6 months
- □ *Dalam 6 – 12 bulan* / Within the past 6-12 months
- □ *Dalam 1 – 5 tahun terakhir* / Sometime in the last 1 - 5 years
- □ *Dalam 5 -10 tahun terakhir* / Sometime in the last 5 - 10 years
- □ *Tidak pernah* / Never

36. *Berapa kerapkah anda membuat ujian paras gula di rumah?* / How often do you do finger-pricks to check your blood glucose?
- □ *Lebih 4 kali sehari* / More than 4 times a day
- □ *3 hingga 4 kali sehari* / 3 to 4 times a day
- □ *1 hingga 2 kali sehari* / 1 to 2 times a day
- □ *Beberapa kali seminggu* / Several times a week
- □ *Saya jarang atau tidak pernah memeriksa paras gula di rumah* / I rarely or never check blood glucose

Nurse Questionnaire for All Patients with Diabetes who Inject

1. What type of diabetes does this patient have?
- □ Type 1
- □ Type 2
- □ Gestational

2. Insulin(s) used by patient (tick all relevant answers):
- □ Short-acting human (R or Regular)
- □ Rapid-acting analogue
- □ NPH
- □ Long-acting analogue (Levemir [detemir] or Lantus [glargine])
- □ Pre-mix human or analogue

3. What other oral Anti-diabetic agents (OAD) patient has, if any; (tick all that apply)
- □ Biguanides (Metformin)
- □ Sulphonylureas (Glibenclamide, Glicazide, Glipizide, Glimepiride)
- □ Meglitinides (Repaglinide, Nateglinide)
- □ Alpha-Glucosidase Inhibitors (Acarbose)
- □ Thiazolidinediones (Rosiglitazone, Pioglitazone)
- □ Dipeptyl Peptidase-4 Inhibitor (DPP-4) (Sitagliptin, Vitagliptin, Saxagliptin, Linagliptin, Alogliptin)
- □ Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors (Dapagliflozin, Canagliflozin, Empagliflozin)

4. Total daily dose of each of insulins used (add all units given currently in one day of each kind of insulin and write total after appropriate insulin)
- □ Short-acting human _____ (total/day)
- □ Rapid-acting analogue _____ (total/day)
- □ NPH _____ (total/day)
- □ Long-acting analogue _____ (total/day)
- □ Pre-mix human or analogue _____ (total/day)

5. Total daily dose (add all the above) _____ (total/day)

6. After examination of the patient, please give your assessment of the **visual appearance** of injection sites (tick as appropriate):

	Normal	Presence of Lipohypertrophy	Presence of Lipoatrophy	Inflamed/ Red or Swollen
Abdomen	□	□	□	□
Thigh	□	□	□	□
Buttocks	□	□	□	□
Arm	□	□	□	□

7. After **palpation**, please give your assessment of the injection sites and measure the diameter of any abnormalities **in mm**:

	Normal	Presence of Lipohypertrophy? If yes, specify size (mm)	Presence of Lipoatrophy? If yes, specify size (mm)
Abdomen	□	□	□
Thigh	□	□	□
Buttocks	□	□	□
Arm	□	□	□

8. Reviewing questions 6 and 7 above, have you found lipohypertrophy visually and/or by palpation at any site on this patient?
- □ Yes
- □ No

9. If the patient has lipohypertrophy does he/she inject into it?
- □ Yes
- □ No

10. If Yes, with what frequency?
- □ Every injection
- □ Frequently (daily)
- □ Occasionally (weekly)
- □ Seldom (monthly)

11. Does the patient rotate his/her injection sites with each injection?
- □ Yes
- □ No

12. Please ask the patient to show you how he/she rotates. Based on this, does the patient practice **correct site rotation** (always injecting at least 1 cm from their previous injection[s])?
- □ Yes
- □ No

13. What was the patient's most recent HbA1c value_____%

14. From your observation of the patient's blood glucose values, would he/she qualify as having **'frequent unexplained hypoglycemia'***?
- □ Yes
- □ No

***'Hypoglycemia' is defined as the occurrence of ≥1 symptom of low sugar (e.g., palpitations, tiredness, sweating, strong hunger, dizziness, tremor) or a confirmed blood glucose meter reading ≤60 mg/dL (3.3 mM/L). 'Frequent unexplained hypoglycemia' is defined as hypoglycemia occurring one or more times weekly in the absence of a definable precipitating event such as a change in medication, diet or activity.**

15. From your observation of the patient's blood glucose values, would he/she qualify as having **'glycemic variability'****?
- □ Yes
- □ No

****'Glycemic variability' is the presence of blood glucose oscillations from less than 60 mg/dL (3.3 mM/L) to more than 250 mg/dL (13.9 mM/L) at least 3 times a week in an unpredictable and unexplained fashion and evidence of such a pattern for at least the previous 6 months**